

\$%^STN;HighlightOn= **;HighlightOff=** ;

Welcome to STN International! Enter x:x

LOGINID:ssspta1633cxq

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?:2

***** Welcome to STN International *****

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Jan 25 BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3 Jan 29 FSTA has been reloaded and moves to weekly updates
NEWS 4 Feb 01 DKLIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6 Mar 08 Gene Names now available in BIOSIS
NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TRCTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12 Apr 08 "Ask CAS" for self-help around the clock
NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14 Apr 09 ZDB will be removed from STN
NEWS 15 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 19 May 31 PCTFULL to be reloaded. File temporarily unavailable.
NEWS 20 Jun 03 New e-mail delivery for search results now available

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

***** STN Columbus *****

FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002

=> FIL BIOSIS EMBASE CAPLUS
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'BIOSIS' ENTERED AT 11:19:22 ON 06 JUN 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 11:19:22 ON 06 JUN 2002
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE 'CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s fertility (3a) treat?
L1 2613 FERTILITY (3A) TREAT?

=> s contracept?
L2 78848 CONTRACEPT?

=> s l1 or l2
L3 81300 L1 OR L2

=> s endometrium (3a) matur?
L4 142 ENDOMETRIUM (3A) MATUR?

=> s l3 or l4
L5 81423 L3 OR L4

=> s l4 and l3
L6 19 L4 AND L3

=> s progest? (3a) receptor?
L7 29173 PROGEST? (3A) RECEPTOR?

=> s (antagonist or inhibit?) (3a) l7
L8 1077 (ANTAGONIST OR INHIBIT?) (3A) L7

=> d bib abs

L8 ANSWER 1 OF 1077 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:325545 BIOSIS

DN PREV200200325545

TI The histone deacetylase ***inhibitor*** trichostatin A blocks
progesterone ***receptor***-mediated transactivation of the
mouse mammary tumor virus promoter in vivo.

AU Wilson, Melissa A.; Ricci, Andrea r.; Deroo, Bonnie J.; Archer, Trevor K.
(1)

CS (1) Chromatin and Gene Expression Section, Lab. of Reproductive and
Developmental Toxicology, NIEHS, NIH, 111 Alexander Dr., MD E4-06,
Research Triangle Park, NC, 27709; archer1@niehs.nih.gov USA

SO Journal of Biological Chemistry, (April 26, 2002) Vol. 277, No. 17, pp.
15171-15181. <http://www.jbc.org/>. print.

ISSN: 0021-9258.

DT Article

LA English

AB Post-translational modifications of histones play an important role in
modulating gene transcription within chromatin. We used the mouse mammary
tumor virus (MMTV) promoter, which adopts an ordered nucleosomal
structure, to investigate the impact of a specific inhibitor of histone
deacetylase, trichostatin A (TSA), on progesterone receptor-activated
transcription. TSA induced global histone hyperacetylation, and this
effect occurred independently of the presence of hormone. Interestingly,
chromatin immunoprecipitation analysis revealed no significant change in
the level of acetylated histones associated with the MMTV promoter
following high TSA treatment. In human breast cancer cells, in which the
MMTV promoter adopts a constitutively "open" chromatin structure,
treatment with TSA converted the MMTV promoter into a closed structure.
Addition of hormone did not overcome this TSA-induced closure of the
promoter chromatin. Furthermore, TSA treatment resulted in the eviction of
the transcription factor nuclear factor-1 from the promoter and reduced
progesterone receptor-induced transcription. Kinetic experiments revealed
that a loss of chromatin-remodeling protein was coincident with the
decrease in MMTV transcriptional activity and the imposition of repressed
chromatin architecture at the promoter. These results demonstrate that
deacetylase inhibitor treatment at levels that induce global histone
acetylation may leave specific regulatory regions relatively unaffected
and that this treatment may lead to transcriptional inhibition by
mechanisms that modify chromatin-remodeling proteins rather than by
influencing histone acetylation of the local promoter chromatin structure.

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002) —

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002

L1 2613 S FERTILITY (3A) TREAT?
L2 78848 S CONTRACEPT?
L3 81300 S L1 OR L2
L4 142 S ENDOMETRIUM (3A) MATUR?
L5 81423 S L3 OR L4
L6 19 S L4 AND L3
L7 29173 S PROGEST? (3A) RECEPTOR?
L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7

=> s 17 alpha fluoralkyl?
L9 0 17 ALPHA FLUORALKYL?

=> s 17 fluoralkyl?
L10 0 17 FLUORALKYL?

=> s 17 (3a) fluoro?
L11 8 17 (3A) FLURO?

=> d bib abs

L11 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1997:83613 BIOSIS

DN PREV199799375326

TI Radiofrequency ablation in multiple accessory pathways.

AU Iturralde Torres, Pedro; Lara, Susano; Picos Bovio, Eva; Colin Lizalde,
Luis; Kershenovich, Sergio; Gonzalez Hermosillo, J. Antonio

CS Inst. Nac. Cardiol., Dep. Electrofisiol., Juan Badiano Number 1, 14080
Mexico, DF Mexico

SO Archivos del Instituto de Cardiologia de Mexico, (1996) Vol. 66, No. 5,
pp. 390-399.

ISSN: 0365-3080.

DT Article

LA Spanish

SL Spanish; English; French

AB Radiofrequency ablation were performed in 465 consecutive patients with Wolff-Parkinson-White syndrome. We demonstrated evidence of multiple accessory pathways in 18 patients (3.9%); 17 had two, and one had three accessory pathways. In three of these there was additional right atrio-fascicular connection. There were 27 manifest and 10 concealed accessory pathways. Six patients had Ebstein's anomaly associated with accessory pathways. The location of the accessory pathways was in the right posterior portion of the ventricular septum in 16, the left posterior portion of the ventricular septum in 5, the right free wall in 5, the left free wall in 7, the right anteroseptal in 3, the midseptum in 1, and one right anterolateral. Of the 37 pathways, 32 (86%) accessory pathways were ablated successfully without complications. Duration of the procedure was 100+58 minutes, and ***fluoscopic*** time 40+-17*** minutes. The mean applications were 26+17 and the power level of the radiofrequency current 41+6 W. A follow-up of 80+40 days after ablation demonstrated incidence of recurrent conduction in 3 accessory pathways (8%). In conclusion, patients with multiple accessory pathways can be treated by radiofrequency ablation in a single session with a high success rate although slightly less than that inpatients with a single accessory pathway.

fluoscopic minutes. The mean applications were 26+17 and the power level of the radiofrequency current 41+6 W. A follow-up of 80+40 days after ablation demonstrated incidence of recurrent conduction in 3 accessory pathways (8%). In conclusion, patients with multiple accessory pathways can be treated by radiofrequency ablation in a single session with a high success rate although slightly less than that inpatients with a single accessory pathway.

=> s 17 (3A) fluor?
L12 3684 17 (3A) FLUOR?

=> s l12 (3a) alkyl?
L13 15 L12 (3A) ALKYL?

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002
L1 2613 S FERTILITY (3A) TREAT?
L2 78848 S CONTRACEPT?
L3 81300 S L1 OR L2
L4 142 S ENDOMETRIUM (3A) MATUR?
L5 81423 S L3 OR L4
L6 19 S L4 AND L3
L7 29173 S PROGEST? (3A) RECEPTOR?
L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7
L9 0 S 17 ALPHA FLUORALKYL?
L10 0 S 17 FLUORALKY?
L11 8 S 17 (3A) FLURO?
L12 3684 S 17 (3A) FLUOR?
L13 15 S L12 (3A) ALKYL?
L14 0 S L13 AND L8
L15 69 S L8 AND L3
L16 1 S L15 AND L6

=> s l13 and l8
L14 0 L13 AND L8

=>

=> s l8 and l3
L15 69 L8 AND L3

=> s l15 and l6
L16 1 L15 AND L6

=> d bib abs

L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2000:854126 CAPLUS

DN 134:37152

TI The use of progesterone antagonists and progesterone receptor modulators in ***contraception***

AU Spitz, I. M.; Van Look, P. F. A.; Coelingh Bennink, H. J. T.

CS Institute of Hormone Research, Shaare Zedek Medical Center, Jerusalem, Israel

SO Steroids (2000), 65(10-11), 817-823
CODEN: STEDAM; ISSN: 0039-128X

PB Elsevier Science Inc.

DT Journal; General Review

LA English

AB A review, with 59 refs. Progesterone antagonists (PAs) and progesterone receptor modulators (PRMs) have ***contraceptive*** potential by suppressing follicular development, delaying the surge of LH, retarding endometrial maturation, and promoting endometrial bleeding. Mifepristone, in daily doses of 2-10 mg, blocks the LH surge and ovulation. Many of the studies were conducted in women not at risk of pregnancy, and thus the ***contraceptive*** efficacy is not yet known. Nevertheless, there is evidence that daily doses of 2 or 5 mg of mifepristone have ***contraceptive*** potential. Because of anovulation, there may be an unopposed estrogen effect on the endometrium, although this risk may be mitigated by the noncompetitive anti-estrogenic activity exhibited by both PAs and PRMs. Low doses of PAs and PRMs, which do not affect ovulation, retard endometrial ***maturation***, indicating that the

endometrium is exquisitely sensitive to these compds. This raises the prospect of endometrial ***contraception***, i.e. prevention of endometrial maturation without disturbing ovulation or producing

alterations in bleeding patterns. This approach works well in monkeys but was not found to be very promising when given to women not using ***contraception***. On the other hand, 200 mg mifepristone administered 48 h after the LH surge, which has minimal or no effect on ovulation and bleeding patterns, is an effective ***contraceptive***; yet, it is not a practical approach to ***contraception***. Late luteal phase administration of mifepristone produces menstrual bleeding. However, when mifepristone was administered every month at the end of the cycle either alone or together with prostaglandins, it was not very effective in preventing pregnancy. In contrast, a mifepristone-prostaglandin combination has been shown to be a very effective treatment for occasional menstrual regulation, with vaginal bleeding induced in 98% of pregnant women, with menses delay of 11 days or less. Mifepristone is an excellent agent for emergency ***contraception*** when used within 120 h of unprotected intercourse. It is also possible that PAs and PRMs may be used to reduce the occurrence of bleeding irregularities induced by progestin-only ***contraceptive*** methods. Both classes of progesterone receptor ligands may also have ***contraceptive*** efficacy by having a pharmacol. effect on the embryo or altering tubal transport or other aspects of tubal physiol.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002
L1 2613 S FERTILITY (3A) TREAT?
L2 78848 S CONTRACEPT?
L3 81300 S L1 OR L2
L4 142 S ENDOMETRIUM (3A) MATUR?
L5 81423 S L3 OR L4
L6 19 S L4 AND L3
L7 29173 S PROGEST? (3A) RECEPTOR?
L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7
L9 0 S 17 ALPHA FLUORALKYL?
L10 0 S 17 FLUORALKY?
L11 8 S 17 (3A) FLURO?
L12 3684 S 17 (3A) FLUOR?
L13 15 S L12 (3A) ALKYL?
L14 0 S L13 AND L8
L15 69 S L8 AND L3
L16 1 S L15 AND L6

=> s conception?
L17 33312 CONCEPTION?

=> s l17 or l1
L18 35752 L17 OR L1

=> s l18 and l4 and l8
L19 0 L18 AND L4 AND L8

=> s l8 and l4
L20 1 L8 AND L4

=> d bib abs

L20 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2000:854126 CAPLUS

DN 134:37152

TI The use of progesterone antagonists and progesterone receptor modulators in ***contraception***

AU Spitz, I. M.; Van Look, P. F. A.; Coelingh Bennink, H. J. T.

CS Institute of Hormone Research, Shaare Zedek Medical Center, Jerusalem, Israel

SO Steroids (2000), 65(10-11), 817-823
CODEN: STEDAM; ISSN: 0039-128X

PB Elsevier Science Inc.

DT Journal; General Review

LA English

AB A review, with 59 refs. Progesterone antagonists (PAs) and progesterone receptor modulators (PRMs) have contraceptive potential by suppressing follicular development, delaying the surge of LH, retarding endometrial maturation, and promoting endometrial bleeding. Mifepristone, in daily doses of 2-10 mg, blocks the LH surge and ovulation. Many of the studies were conducted in women not at risk of pregnancy, and thus the contraceptive efficacy is not yet known. Nevertheless, there is evidence that daily doses of 2 or 5 mg of mifepristone have contraceptive potential. Because of anovulation, there may be an unopposed estrogen effect on the endometrium, although this risk may be mitigated by the noncompetitive anti-estrogenic activity exhibited by both PAs and PRMs. Low doses of PAs and PRMs, which do not affect ovulation, retard endometrial ***maturation***, indicating that the ***endometrium*** is exquisitely sensitive to these compds. This raises the prospect of endometrial contraception, i.e. prevention of endometrial maturation without disturbing ovulation or producing alterations in bleeding patterns. This approach works well in monkeys but was not found to be very promising when given to women not using contraception. On the other hand, 200 mg mifepristone administered 48 h after the LH surge, which has

minimal or no effect on ovulation and bleeding patterns, is an effective contraceptive; yet, it is not a practical approach to contraception. Late luteal phase administration of mifepristone produces menstrual bleeding. However, when mifepristone was administered every month at the end of the cycle either alone or together with prostaglandins, it was not very effective in preventing pregnancy. In contrast, a mifepristone-prostaglandin combination has been shown to be a very effective treatment for occasional menstrual regulation, with vaginal bleeding induced in 98% of pregnant women, with menses delay of 11 days or less. Mifepristone is an excellent agent for emergency contraception when used within 120 h of unprotected intercourse. It is also possible that PAs and PRMs may be used to reduce the occurrence of bleeding irregularities induced by progestin-only contraceptive methods. Both classes of progesterone receptor ligands may also have contraceptive efficacy by having a pharmacological effect on the embryo or altering tubal transport or other aspects of tubal physiology.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002

L1 2613 S FERTILITY (3A) TREAT?
 L2 78848 S CONTRACEPT?
 L3 81300 S L1 OR L2
 L4 142 S ENDOMETRIUM (3A) MATOR?
 L5 81423 S L3 OR L4
 L6 19 S L4 AND L3
 L7 29173 S PROGEST? (3A) RECEPTOR?
 L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7
 L9 0 S 17 ALPHA FLUORALKYL?
 L10 0 S 17 FLUORALKYL?
 L11 8 S 17 (3A) FLURO?
 L12 3684 S 17 (3A) FLUOR?
 L13 15 S L12 (3A) ALKYL?
 L14 0 S L13 AND L8
 L15 69 S L8 AND L3
 L16 1 S L15 AND L6
 L17 33312 S CONCEPTION?
 L18 35752 S L17 OR L1
 L19 0 S L18 AND L4 AND L8
 L20 1 S L8 AND L4

=> dup rem l6

PROCESSING COMPLETED FOR L6

L21 8 DUP REM L6 (11 DUPLICATES REMOVED)

=> d bib abs -1

YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L21 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
 INC.DUPLICATE 1

AN 2001:45304 BIOSIS
 DN PREV200100045304

TI The use of progestin antagonists and progesterone receptor modulators in ***contraception***.

AU Spitz, Irving M. (1); Van Look, Paul F. A.; Coelingh Bennink, Herjan J. T. CS (1) Institute of Hormone Research, Shaare Zedek Medical Center, Jerusalem; spitz@popcrb.rocketfeller.edu Israel
 SO Steroids, (October November, 2000) Vol. 65, No. 10-11, pp. 817-823. print. ISSN: 0039-128X.

DT Article

LA English

SL English

AB Progesterone antagonists (PAs) and progesterone receptor modulators (PRMs)

have ***contraceptive*** potential by suppressing follicular development, delaying the surge of luteinizing hormone (LH), retarding endometrial maturation, and promoting endometrial bleeding. Mifepristone, in daily doses of 2-10 mg, blocks the LH surge and ovulation. Many of the studies were conducted in women not at risk of pregnancy, and thus the ***contraceptive*** efficacy is not yet known. Nevertheless, there is evidence that daily doses of 2 or 5 mg of mifepristone have

contraceptive potential. Because of anovulation, there may be an unopposed estrogen effect on the endometrium, although this risk may be mitigated by the noncompetitive anti-estrogenic activity exhibited by both PAs and PRMs. Low doses of PAs and PRMs, which do not affect ovulation, retard endometrial ***maturation***, indicating that the

endometrium is exquisitely sensitive to these compounds. This raises the prospect of endometrial ***contraception***, i.e. prevention of endometrial maturation without disturbing ovulation or producing alterations in bleeding patterns. This approach works well in monkeys but was not found to be very promising when given to women not using ***contraception***. On the other hand, 200 mg mifepristone administered 48 h after the LH surge, which has minimal or no effect on ovulation and bleeding patterns, is an effective ***contraceptive***; yet, it is not a practical approach to ***contraception***. Late luteal phase administration of mifepristone produces menstrual bleeding. However, when mifepristone was administered every month at the end of the

cycle either alone or together with prostaglandins, it was not very effective in preventing pregnancy. In contrast, a mifepristone-prostaglandin combination has been shown to be a very effective treatment for occasional menstrual regulation, with vaginal bleeding induced in 98% of pregnant women, with menses delay of 11 days or less. Mifepristone is an excellent agent for emergency ***contraception*** when used within 120 h of unprotected intercourse. It is also possible that PAs and PRMs may be used to reduce the occurrence of bleeding irregularities induced by progestin-only contraceptive methods. Both classes of progesterone receptor ligands may also have ***contraceptive*** efficacy by having a pharmacological effect on the embryo or altering tubal transport or other aspects of tubal physiology.

L21 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
 INC.DUPLICATE 2

AN 1998:173048 BIOSIS

DN PREV199800173048

TI Vascular endothelial growth factor is essential for corpus luteum angiogenesis.

AU Ferrara, Napoleone (1); Chen, Helen; Davis-Smyth, Terri; Gerber, Hans-Peter; Thuy-Nhung Nguyen; Peers, David; Chisholm, Vanessa; Hillan, Kenneth J.; Schwall, Ralph H.

CS (1) Dep. Cardiovasc. Res., Process Sci. Pathol. Mol. Oncol., Genentech Inc., 1 DNA Way, San Francisco, CA 94080 USA

SO Nature Medicine, (March, 1998) Vol. 4, No. 3, pp. 336-340.

ISSN: 1078-8956.

DT Article

LA English

AB The development and endocrine function of the ovarian corpus luteum (CL) are dependent on the growth of new capillary vessels. Although several molecules have been implicated as mediators of CL angiogenesis, at present there is no direct evidence for the involvement of any. Here we report the unexpected finding that treatment with truncated soluble Flt-1 receptors, which inhibit vascular endothelial growth factor (VEGF) bioactivity, resulted in virtually complete suppression of CL angiogenesis in a rat model of hormonally induced ovulation. This effect was associated with inhibition of CL development and progesterone release. Failure of ***maturation*** of the ***endometrium*** was also observed. Areas of ischemic necrosis were demonstrated in the corpora lutea (CLs) of treated animals. However, no effect on the preexisting ovarian vasculature was observed. These findings demonstrate that, in spite of the redundancy of potential mediators, VEGF is essential for CL angiogenesis. Furthermore, they have implications for the control of ***fertility*** and the ***treatment*** of ovarian disorders characterized by hypervascularity and hyperplasia.

L21 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
 INC.DUPLICATE 3

AN 1997:117292 BIOSIS

DN PREV199799416495

TI Midluteal immunoreactive alpha-inhibin serum concentrations as markers of luteal phase deficiency.

AU Balash, Juan (1); Creus, Montserrat; Fabregues, Francisco; Casamitjana, Roser; Ordi, Jaime; Vanrell, Juan A.

CS (1) Dep. Obstet. Gynaecol., Fac. Med.-Univ. Barcelona, Barcelona Spain

SO Human Reproduction (Oxford), (1996) Vol. 11, No. 12, pp. 2591-2594.

ISSN: 0268-1161.

DT Article

LA English

AB The present prospective clinical study was undertaken to determine the usefulness of midluteal phase serum immunoreactive alpha-inhibin concentrations as markers of luteal phase deficiency and whether they are better indicators of biopsy confirmed luteal phase defect than serum progesterone. Consecutive patients (n = 138) with regular menstrual cycles attending our Infertility Clinic (experimental group) and 5 fertile women who were requesting ***contraception*** and had regular menstrual patterns (control group) were included. In all women (patients and controls), basal body temperature, midluteal serum concentrations of oestradiol, prolactin, progesterone and immunoreactive alpha-inhibin, and premenstrual endometrial biopsy were used in the same cycle to assess luteal function. Out-of-phase secretory endometria were detected in 15 of the 138 patients. Thus, hormonal concentrations were compared between the following three groups of women: group 1 (n = 15), infertile patients with defective secretory endometria; group 2 (n = 123), infertile patients with normal secretory endometria; and controls (n = 15), fertile women with normal secretory endometria. Midluteal serum concentrations of progesterone, immunoreactive alpha-inhibin, oestradiol, and prolactin of the two groups studied were similar to those of the control group of fertile women. Our results indicate that midluteal serum inhibin determination does not accurately reflect histological ***maturation*** of the ***endometrium*** and it is not a better indicator of endometrial luteal phase deficiency than midluteal serum progesterone concentration.

L21 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS
 INC.DUPLICATE 4

AN 1994:537392 BIOSIS

DN PREV199497550392

TI The effect of antiprogestin (RU 486) and prostaglandin biosynthesis inhibitor (naproxen) on uterine fluid prostaglandin F-2-alpha concentrations.

AU Gemzell-Danielsson, Kristina (1); Hamberg, Mats

CS (1) Dep. Obstet. Gynaecol., Karolinska Hosp., S-171 76 Stockholm Sweden

SO Human Reproduction (Oxford), (1994) Vol. 9, No. 9, pp. 1626-1630.

ISSN: 0268-1161.

DT Article

LA English

AB In the present study the effect of the antiprogestin RU 486 and the prostaglandin biosynthesis inhibitor, naproxen, on uterine fluid concentration of prostaglandin F-2alpha (PGF-2alpha) was investigated. RU 486, 200 mg, was administered two days after the luteinizing hormone (LH) surge and naproxen, 500 mg, was given every 12th hour five times starting 4 days after the LH surge. Uterine fluid was collected in the proliferative phase at ovulation and in the mid-luteal phase in a control and treatment cycle. The amount of PGF-2alpha was measured by gm chromatography-mass spectrometry. In the control cycle, the highest concentration of PGF-2alpha was found in the mid-luteal phase, and the lowest at the time of ovulation. Both RU 486 and naproxen reduced the PGF-2alpha concentration in uterine fluid considerably, or to 22-25% of that in the control cycle at the time of implantation. PGF-2alpha produced by the endometrium is believed to be of importance for the implantation of the blastocyst. Postovulatory treatment with RU 486 effectively prevents implantation, probably mainly by inhibiting the ***maturation*** of the ***endometrium*** during the secretory phase of the cycle. It is suggested that the inhibition of PGF-2alpha release through the uterine fluid caused by RU 486 may also be of importance.

L21 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5

AN 1989:430476 BIOSIS

DN BA88:88734

TI ***CONTRACEPTIVE*** POTENTIAL OF RU-486 BY OVULATION

INHIBITION I.

PITUITARY VERSUS OVARIAN ACTION WITH BLOCKAGE OF ESTROGEN-INDUCED

ENDOMETRIAL PROLIFERATION.

AU VAN UEM J F H M; HSIU J G; CHILLIK C F; DANFORTH D R; ULMANN A; BAULIEU E

E; HODGEN G D

CS JONES INST. REPRODUCTIVE MED., DEP. OBSTET. GYNECOL.,

EASTERN VA. MED.

SCH., 855 WEST BRAMBLETON AVE., SUITE B, NORFOLK, VA. 23510.

SO CONTRACEPTION, (1989) 40 (2), 171-184.

CODEN: CCPTAY. ISSN: 0010-7824.

FS BA; OLD

LA English

AB In previous studies, RU 486 administration arrested spontaneous folliculogenesis. To investigate the central versus peripheral effects of RU 486 on the ovarian/menstrual cycle, including endometrial proliferation, RU 486 was administered daily (10 mg/kg/day, im) from menstrual cycle day 3 or 7 to day 25 in normal adult cynomolgus monkeys receiving hMG treatment (37.5 IU/day) from days 3-8 (n = 6). RU 486 administration with hMG/hCG therapy did not inhibit ovarian response, as evidenced by steroidogenesis and ovulation. Nine of 23 oocytes retrieved by lavage or follicular aspiration at laparotomy after ovulation induction were morphologically classified as mature preovulatory status. Whereas an endometrial biopsy performed on cycle day 25 in control monkeys revealed an in phase ***mature*** secretory ***endometrium***, histologic sections from RU 486 plus hMG/hCG treated females uniformly demonstrated atrophic to weakly proliferative endometrium on cycle day 25, despite serum estradiol levels > 300 pg/ml. Three months after the initial 25-day study endometrial biopsies revealed persistent atrophic endometrium, even though repeated ovulation induction with hMG/hCG therapy elevated serum estrogen concentrations. The finding prevailed whether RU 486 treatment began on cycle day 3 or 7. The intermenstrual interval was significantly (P < 0.01) lengthened by RU 486 treatments (28.5. +/- 2.0, control vs 131.3. +/- 11.5 days, RU 486). In summary, RU 486 consistently blocked ovulation unless hCG was provided and elicited a persistent retardation of early proliferative endometrium when administered daily beginning in early or mid-follicular phase. The normal mitogenic effects of elevated ovarian estrogen secretion on endometrial tissue were quelled, uniformly resulting in amenorrhea. The long-lasting action of RU 486, causing ovulation inhibition and atrophic endometrium, may be due to the depot effect of im injection. In addition, RU 486 did not prevent ovarian steroidogenesis, ovulation or oocyte maturation when an ovulation induction regimen of hMG/cCG was given. These findings show that RU 486 prevented ovulation by diminishing pituitary gonadotropin secretion, rather than by direct effects on ovarian folliculogenesis, and induced amenorrhea by inhibiting estrogen-induced endometrial proliferation.

L21 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6

AN 1988:74501 BIOSIS

DN BA85:40800

TI ENDOMETRIAL HISTOLOGY DURING INTERMITTENT INTRANASAL LHRH AGONIST

SEQUENTIALLY COMBINED WITH AN ORAL PROGESTOGEN AS AN ANTIOVULATORY

CONTRACEPTIVE APPROACH.

AU LEMAY A; JEAN C; FAURE N

CS CENTRE DE RECHERCHE ET DEP. DE GYNECOLOGIE-OBSTETRIQUE.

SO FERTIL STERIL, (1987) 48 (5), 775-782.

CODEN: FESTAS. ISSN: 0015-0282.

FS BA; OLD

LA English

AB Endometrial biopsies were performed in four groups of six or seven women

treated for periods of 14 or 21 days with 200 .mu.g twice daily or 400 .mu.g once daily or intranasal Buserelin acetate. Five milligrams of medroxyprogesterone acetate (MPA) was taken orally twice daily on days 15 to 21. A medication-free week followed each treatment period. Between days 12 and 15 of the first treatment cycle, a proliferative endometrium was described in 16 out of 24 biopsies (66%). In 8 specimens (33%), early secretory changes were related to an early and/or short-lived rise in serum progesterone (P). At the end of the fourth treatment cycle, advanced maturation (days 23 to 28) was observed mainly in the 14-day schedules where serum estradiol (E2) was stimulated in or above the normal range of control cycles. Early to midluteal phase dating (days 16 to 22) was described mainly in the 21-day schedules. There was no P elevation in these groups. Five biopsies showing only proliferative tissue were associated with low levels of E2 mainly in the 400 .mu.g/day group. The regimen capable of maintaining E2 in the low physiologic range (200 .mu.g/12 hours .times. 21 days) was associated with incomplete secretory changes of the endometrium. A longer period of progestogen administration should produce a more complete ***maturation*** of the ***endometrium***.

L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1976:504445 CAPLUS

DN 85:10445

TI Fructose metabolism in the rat endometrium under normal and experimental conditions

AU Boshier, D. P.; Katz, June M.

CS Dep. Anat., Univ. Auckland, Auckland, N. Z.

SO J. Reprod. Fertil. (1976), 47(2), 245-9

CODEN: JRPFA4

DT Journal

LA English

GI

/ Structure 1 in file .gra /

AB Fructose 1,6-diphosphate (FDP) [488-69-7] hydrolysis, which was measured in tissue exts. from ***mature*** rat ***endometrium***, was maximal during late diestrus and early proestrus and reflected the variations in the plasma levels of ovarian steroids. Treatment of ovariectomized animals with estradiol benzoate (I benzoate) [50-50] or medroxyprogesterone acetate [71-58-9] increased FDP hydrolysis when compared with control animals, although I was the more effective. FDP hydrolysis was greater in exts. of endometrial tissue from uterine horns contg. a silk IUD or of deciduomata tissue from pseudopregnant rats, in which the peak was on day 9, than in exts. of endometrium from the control contralateral horn. The linking of glycogen metab. in normal endometrium, IUD-contg. horns, and decidua tissue to the role of FDP in gluconeogenesis and the promotion of glycogen storage is discussed.

L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1971:120826 CAPLUS

DN 74:120826

TI Activators of coagulation and fibrinolytic systems in normal and drug-influenced [menstrual] cycles

AU Stein, W. W.; Halberstadt, E.; Schwedes, R.

CS Univ.-Frauenklin., Frankfurt/M., Ger.

SO Fortschr. Med. (1971), 89(1), 17-20, 40

CODEN: FMDZAR

DT Journal

LA German

AB In addn. to thromboplastic activity, which showed no cyclic changes, the ***endometrium*** of sexually ***mature*** females was found to contain fibrinolytic activity, predominantly an activator which converts plasminogen into plasmin. The concn. of this activator increased in the menstrual secretion phase. Activator activity, but not thromboplastic activity, decreased during treatment with estrogen-gestagen preps. Treatment with synthetic antifibrinolytics almost completely eliminated tissue activator activity.

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002

L1 2613 S FERTILITY (3A) TREAT?

L2 78848 S CONTRACEPT?

L3 81300 S L1 OR L2

L4 142 S ENDOMETRIUM (3A) MATUR?

L5 81423 S L3 OR L4

L6 19 S L4 AND L3

L7 29173 S PROGEST? (3A) RECEPTOR?

L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7

L9 0 S 17 ALPHA FLUORALKYL?

L10 0 S 17 FLUORALKYL?

L11 8 S 17 (3A) FLURO?

L12 3684 S 17 (3A) FLUOR?

L13 15 S L12 (3A) ALKYL?

L14 0 S L13 AND L8

L15 69 S L8 AND L3

L16 1 S L15 AND L6

L17 33312 S CONCEPTION?
 L18 35752 S L17 OR L1
 L19 0 S L18 AND L4 AND L8
 L20 1 S L8 AND L4
 L21 8 DUP REM L6 (11 DUPLICATES REMOVED)

=> dup rem l13
 PROCESSING COMPLETED FOR L13
 L22 15 DUP REM L13 (0 DUPLICATES REMOVED)

=> d bib abs 1-
 YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L22 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
 AN 2000:750323 CAPLUS

DN 133:321996

TI Preparation of chlorosilanes

IN Chang, Il Nam; Yoo, Bok Yeul; Cho, Yeun Sok; Hahn, Joon soo
 PA Korea Institute of Science and Technology, S. Korea
 SO Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 2000297091 A2 20001024 JP 2000-15275 20000125
 KR 2000066127 A 20001115 KR 1999-13006 19990413
 PRAI KR 1999-13006 A 19990413
 OS CASREACT 133:321996; MARPAT 133:321996
 AB R4C2SiR1C12 (R1 = H, Cl, C1-6 ***alkyl***, Ph; R4 = C1- ***17*** ***alkyl***, C1-10 ***fluoroalkyl***, C2-5 alkaryl, (CH2)nSiMe3-mClm, (substituted) arom. hydrocarbyl, (CH2)pSiR1C12, ArCH2SiR1C12; Ar = C6-14 arom. hydrocarbyl; n = 0-2; m = 0-3; p = 0-9) are prep'd. by dehydrohalogenation of HSiR1C12 (R1 = same as above) with R2CH2X
 [R2 = C1- ***17*** ***alkyl***, C1-10 ***fluoroalkyl***, C2-5 alkaryl, (CH2)nSiMe3-mClm, (substituted) arom. hydrocarbyl, halo(alkyl), (halomethyl)aryl; X = Cl, Br; n, m = same as above] in the presence of tertiary phosphines. E.g., 1-chlorohexane was treated with HSiCl3 in the presence of Bu3P to give 65% hexyltrichlorosilane.

L22 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1998:558823 CAPLUS

DN 129:161760

TI Antigestagenerically active steroids with ***fluorinated*** ***17*** alpha.- ***alkyl*** chain

IN Schwede, Wolfgang; Cleve, Arwed; Klar, Ulrich; Neef, Guenter; Chwalisz, Kristof; Schneider, Martin; Fuhmann, Ulrike; Hess-Stumpp, Holger
 PA Schering A.-G., Germany

SO Ger. Offen., 10 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI DE 19706061 A1 19980813 DE 1997-19706061 19970207
 ZA 9800985 A 19990803 ZA 1998-985 19980206
 WO 9834947 A1 19980813 WO 1998-EP752 19980209
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK,
 EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
 NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
 UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG
 AU 9861005 A1 19980826 AU 1998-61005 19980209
 AU 742834 B2 20020110

EP 970103 A1 20000112 EP 1998-905419 19980209

EP 970103 B1 20020417

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 BR 9807667 A 20000215 BR 1998-7667 19980209
 JP 2001510479 T2 20010731 JP 1998-533785 19980209
 NO 9903811 A 19991004 NO 1999-3811 19990806
 US 6316432 B1 20011113 US 2000-516359 20000301
 CN 1324802 A 20011205 CN 2000-129015 20000925
 US 2002045774 A1 20020418 US 2001-978689 20011018

PRAI DE 1997-19706061 A 19970207

US 1998-20947 B1 19980209

WO 1998-EP752 W 19980209

US 2000-516359 XX 20000301

OS MARPAT 129:161760

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA
 OFFLINE PRINT *

AB Title compds. I [R1 = Me, Et; R2 = CnFmHo; n = 2, 3, 4, 5, 6; m > 1; m+o = 2n+1; R3 = (un)etherized OH; R4, R5 = H, or R4R5 = bond, CH2; St = steroidal partial structure Q1-Q3; R6 = H, alkyl, halo; R7 = H, alkyl, or R6R7 = bond when St = Q1 or Q2; X = O, HO-N-, or (H,H); R8 = Y, aryl group (un)substituted by Y; Y = H, halo, OH, NO2, N3, cyano, substituted amino, acyl, etc.] are prep'd. Thus, II was prep'd. in 5 steps from 4-[3,3:17,17-bis(ethylenedioxy)est-5-en-11-beta-]phenol and perfluoronyl fluoride via condensation, deacetalization, addn. reaction with pentafluoroethyl iodide, reaction with (1-ethoxyethenyl)tributylstannane, and hydrolysis-isomerization. In an in vivo test, II at 0.1 mg/animal/day effected a 100% abortion rate in rats.

L22 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1991:138934 CAPLUS

DN 114:138934

TI Modification of endopeptidase for enhancing enzymic activity in organic solvents

IN Kawasaki, Norihiro; Takashita, Katsuhige

PA Sanshin Chemical Industry Co., Ltd., Japan; Snow Brand Milk Products Co., Ltd.

SO Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 02234674 A2 19900917 JP 1989-55053 19890309
 OS MARPAT 114:138934

AB Endopeptidase is modified by introduction of RC(O) groups (e.g. benzyloxy, tert-butoxy, 9- ***fluoromethylmethoxy***, p-methoxybenzyloxy, C1- ***17*** ***alkyl***) into 10-65% of the amino groups on the surface of the enzyme with chems. such as RC(O)OC6H4S(Me)2+CH3SO4-. In org. solvents, the modified enzymes are more stable than the wild type enzyme; therefore, they are useful for peptide synthesis. Modification of chymotrypsin with 4-benzyloxycarbonyloxyphenyl dimethylsulfonium methylsulfate (Z-DSP) was shown. In synthesis of Z-Tyr-Gly-NH2 from benzyloxycarbonyl tyrosine and glycaminide in the presence of 50% DMF (dimethylformamide), the chymotrypsin having 35% of its amino group modified gave 64% prodn.; the unmodified enzyme, contrary, gave 5% prodn. Also given was the modification of trypsin, and again org. solvent-resistance of the modified enzyme was obstd.

L22 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1991:430756 CAPLUS

DN 115:30756

TI Abrasive tapes for finishing of magnetic recording heads

IN Sato, Masami; Fujiyama, Masaaki; Nishikawa, Yasuro; Iwasaki, Takashi
 PA Fuji Photo Film Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 02095578 A2 19900406 JP 1988-247220 19880930
 JP 2588006 B2 19970305

AB The title tapes are prep'd. by forming layers contg. abrasives, binders, and the polyethers R1Z(CH2CHR2O)nH (R1 = C6-30 hydrocarbyl, C1- ***17*** ***fluoroalkyl***; R2 = H, ***alkyl***; Z = O, NH, S, SO2, sulfonylimino; n = 1-30) on flexible substrates. A mixt. of powd. alpha.-Fe203 225, Cr203 75, vinyl chloride polymer (contg. 3.5% epoxy group and 0.5% SO3Na group) 8.3, sulfonated polyurethane 4.8, 3:1 24-TDI-trimethylolpropane adduct 9.6, C16H33O(CH2CH2O)10H, MEK 100, and

cyclohexane 100 parts was coated on a PET film and dried to give a film with a 5-μm.m abrasive layer which could finish a magnetic head in 21 s; vs. 98 with Bu stearate instead of the polyether.

L22 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1988:196001 CAPLUS

DN 108:196001

TI Heat-sensitive recording material contg. phthalide derivative, fluorene derivatives and phenylenediamine derivatives

IN Kanda, Nobuo; Hirahara, Kazuko; Kondo, Mitsuru

PA Kanzaki Paper Mfg. Co., Ltd., Japan

SO Eur. Pat. Appl., 48 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI EP 232907 A2 19870819 EP 1987-101874 19870211
 EP 232907 A3 19880427
 EP 232907 B1 19910327

R: DE, GB
 JP 62184881 A2 19870813 JP 1986-28098 19860212
 JP 05016357 B4 19930304
 JP 63015785 A2 19880122 JP 1986-147775 19860624
 JP 06045264 B4 19940615
 US 4761398 A 19880802 US 1987-11101 19870205

PRAI JP 1986-28098 19860212
JP 1986-147775 19860624

GI For diagram(s), see printed CA Issue.

AB A heat-sensitive recording material comprising, .gtoreq.1 phthalide deriv I
[R1-10 = H, halo, nitro, (substituted) alkyl, (substituted) cycloalkyl,
(substituted) alkoxy, (substituted) acyloxy, (substituted) aryl,
(substituted) phenoxy, (substituted) thioalkoxy, NR12R13 wherein R12, R13
= H, (substituted) alkyl, (substituted) cycloalkyl, (substituted) aryl,
(substituted) aralkyl, tetrahydrofurfuryl, (substituted) acyl; R12 and
R13 may form a hetero ring together or with an adjacent benzene ring; R11
= H, lower alkyl, a, b, c, and d represent C atoms and one or two of them
may be N atom; the C atom may have a substituent selected from H, halo,
alkyl, alkoxy, (substituted) amino, nitro; a-b, b-c, or c-d bond may form
another arom. ring as a basic dye is claimed wherein .gtoreq.1 compd.
selected from ***fluorene*** deriv. II [R14- ***17*** = C18
alkyl, C5-8 cycloalkyl, C3-8 alkoxyalkyl, aryl or aralkyl
(un)substituted with halo, C1-4 alkoxy; R14R15 or R16R17 may form a
hetero ring together or with an adjacent benzene ring; X = H, halo, C1-4
satd. alkyl, C1-4 alkoxyalkyl; NR18R19 wherein R18 and R19 are each same
as R14-17; n = 1-4] and a p-phenylenediamine deriv. III [R20, R21 = C1-10
satd. alkyl, C3-9 unsatd. alkyl, C5-8 cycloalkyl, 3-methacryloyloxy-2-
hydroxypropyl, aralkyl, aryl, arylsulfonyl (un)substituted with halo, C1-4
alkoxy] are further contained in the recording material. The recording
material can be read by an optical character-reading device having a
reading wavelength range over the IR region and has good preservability of
the record images, particularly stable against humidity and heat.

L22 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1986:628976 CAPLUS

DN 105:228976

TI All-purpose sanitary cleaning composition

IN Wenzel, George

PA Sanitary Products Corp., USA

SO U.S., 4 pp. Cont. of U.S. Ser. No. 520,626, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 4612135 A 19860916 US 1985-765578 19850814

PRAI US 1983-520626 19830805

AB A sanitary cleaning compn., capable of cleaning everything in restrooms,
comprises H3PO4 0.12-20, oxalic acid 0.04-9, nonionic surfactant
R(OCH2CH2)nOH (R = alkylaryl, n = 1-20) 0.1- ***17***, cationic
surfactant (***fluorinated*** ***alkyl*** quaternary ammonium
iodide contg. C4-16 alkyl group) 0.03-0.3, glycol ether HOCH2CH2OR (R =
lower alkyl) 0.14-44, and odor-masking agent 0.006-1.7, the balance being
water and H3PO4 being present in excess of the oxalic acid. Thus, a
cleaning compn. contained water 1830.0, 85% H3PO4 195.0, oxalic acid 67.5,
BuOCH2CH2OH 200.0, ethoxylated nonylphenol 120.0, cationic surfactant
(fluorinated alkyl quaternary ammonium iodide) 4.5, and odor-masking agent
(mix of wintergreen, pine oil, geranium crystals, coumaric anhydride,
and turpentine) 9.0 lbs.

L22 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1981:568956 CAPLUS

DN 95:168956

TI Some new membrane labeling agents having a benzacridine structure

AU Jacquignon, Pierre; Viallet, Pierre; Ricci, Adolfo; Bistocchi, Giovanni
Alunni; De Meo, Giovanni; Vigo, Jean; Pedini, Mauro; Binaglia, Luciano

CS Inst. Chim. Subst. Nat., CNRS, Gif-sur-Yvette, 91190, Fr.

SO C. R. Seances Acad. Sci., Ser. 2 (1981), 292(8), 675-8

CODEN: CRSUDO

DT Journal

LA French

GI

/ Structure 2 in file .gra /

AB Dinaphthopyridines I (R = C1- ***17*** ***alkyl***), useful as
fluorescent labeling agents for cell membranes (no data), were
prep'd. from N-(1-naphthyl)-2-naphthylamine (II). A mixt. of EtCO2H, II,
and ZnCl2 was heated 3 h at 220.degree. to give I (R = Et).

L22 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1978:444639 CAPLUS

DN 89:44639

TI Heat stabilizers for halogen-containing resins

IN Tadenuma, Masahiko; Sato, Tamotsu; Tanaka, Kichiji; Shibatsuji, Takeo

PA Akishima Kagaku Kogyo K. K., Japan

SO Japan. Kokai, 8 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 53009847 A2 19780128 JP 1976-84378 19760715

JP 57039260 B4 19820820

GI

/ Structure 3 in file .gra /

AB Halogen-contg. resins are stabilized with I (R = C1-17 alkyl, alkenyl,
aryl, substituted aryl, aralkyl, cycloalkyl, heterocyclic residue; R1 =
C1. ***17*** ***alkyl***, alkenyl, ***fluoroalkyl***, aryl,
substituted aryl, aralkyl, cycloalkyl, PhO, heterocyclic residue; n = 1-5;
M = Group IA, IIA, IIB metal, Zr, Sb). For example, a compn. from PVC
[9002-86-2] 100, DOP 48, epoxidized soybean oil 2, Zn stearate 0.5, Ba
stearate 1.0, and I (R = Bu, R1 = C17H35, n = 2, M = Zn) [66625-88-5] 0.1
part gave a transparent colorless sheet becoming light yellow after 40 min
in a 180.degree. air oven, while a sheet not contg. I became yellowish red
in 20 min.

L22 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
AN 1988:487366 CAPLUS
DN 89:7366

TI Hydrolysis of 9.alpha.-fluoro-11.beta.,21-dihydroxy-16.beta.-methyl-
16.alpha.,17.alpha.-oxidopregna-1,4-diene-3,20-dione 21-acetate

IN Taub, David; Hoffsommer, Robert D., Jr.; Wendler, Norman L.

PA Merck and Co., Inc.

SO U.S., 3 pp. Continuation-in-part of U.S. 3285940

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 3378574 A 19860416 US 1966-538579 19660330

GI For diagram(s), see printed CA Issue.

AB The title compd. was prep'd. from 9.alpha.-fluoro-11.beta.,21-trihydroxy-
16.alpha.-methylpregna-1,4-diene-3,20-dione (I). I disemicarbazone, m.
>300.degree., on acylation with Ac2O in HOAc under reflux 1 hr. gave the
21-acetate. The reaction mixt. was treated with H2O and 5 hrs. on a steam
bath to afford 9.alpha.-fluoro-11.beta.,21-dihydroxy-16.methylpregna-
1,4,16-triene-3,20-dione 21-acetate (II), m. 228-33.degree.. Addn. of 10
g. Na2HPO4 to a stirred soln. of 510 mg. II in 15 ml. CH2Cl2, cooling to
0.degree., addn. of 2.5 moles 2M soln. peroxytrifluoroacetic acid, and
reaction 1 hr. at room temp. gave 9.alpha.-fluoro-11.beta.,21-dihydroxy-
16.alpha.-methyl-16.alpha.,17.alpha.-oxidopregna-1,4-diene-3,20-dione
21-acetate (III). Addn. of 10 ml. 5% HCl in HOAc to 200 mg. III in 10 ml.
HOAc and reaction for 5 min. afforded 9.alpha.-fluoro-
11.alpha.,17.alpha.,21-trihydroxy-16.methylpregna-1,4,15-triene-3,20-dione
21-acetate, 9.alpha.-fluoro-11.beta.,17.alpha.,21-trihydroxy-16-
methylpregna-1,4-diene-3,20-dione 21-acetate, 9.alpha.-fluoro-
11.beta.,21-dihydroxy-16.methylpregna-1,4,14,16-tetraene-3,20-dione
21-acetate, and 9.alpha.-fluoro-15-chloro-11.beta.,21-dihydroxy-16-
methylpregna-1,4,16-triene-3,20-dione 21-acetate. By using HBr in HOAc or
HF in tetrahydrofuran, the corresponding 15-bromo and 9.alpha.,15-difluoro
compds. were obtained.

L22 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1985:489178 CAPLUS

DN 63:89178

OREF 63:16429g-h,16430a-h,16431a-h,16432a-h,16433a-h,16434a-b

TI 10.alpha.-Methyl-9.beta.-hormonal steroids

IN Reerink, Engbert H.; Westerhof, Pieter; Schoeler, Hendrik F. L.

PA North American Phillips Co., Inc.

SO 56 pp.

DT Patent

LA Unavailable

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 3198792 19650803 US 19590408

DE 1228610 DE

AB 4,7,22-Lumistatin-3-one (125 g.) in 2,2,1. iso-PrOH previously satd.
with dry HCl, dry HCl passed through the soln. for 0.5 hr., and worked up
gave 80.5 g. lumista-4,6,22-trien-3-one (I), m. 101-2.degree. (ligno),
[.alpha.]2D-632.degree. (all rotations in CHCl3 unless otherwise
mentioned). I (3 g.) in 300 ml. Et2O added to 450 ml. liquid NH3, treated
with 420 mg. Li in NH3 and the product chromatographed on Al2O3 gave 2.43
g. lumista-4,22-dien-3-one (II), m. 122-4.degree. (Me2CO), [.alpha.]2D
-125.degree.. II (20g.) in 750 ml. CH2Cl2 and 5.75 ml. C5H5N ozonized 4.5
hrs. at -80 gave 10.1 g. 3-oxo retrobisnor-4-cholen-22-ol (III), m.
122-30.degree. (ligno), [.alpha.]2D-144.degree.. III (450 mg.) in 15
ml. CHCl3 and 25 ml. AcOH oxidized 16 hrs. at 30.degree. with 200 mg. CrO3
and 0.2 ml. H2O gave 340 mg. 3-oxoretrobisnor-4-cholenic acid (IV), m.
202-4.degree. (Et2O). Alternatively a soln. of 450 mg. of an ozonide of
II in 25 ml. CH2Cl2 left overnight at 30.degree. with 200 mg. CrO3 in 25
ml. AcOH gave 150 mg. IV. III (300 mg.), 0.11 ml. piperidine, and 1 to 5
mg. p-MeCO4SO3H refluxed 3 hrs. in 5 ml. dry C6H6 gave 185 mg.
22-(N-piperidyl)retrobisnorchola-4,20(22)dien-3-one (V), m. 94-6.degree.
(MeOH). Other samples of V m. 114-15.degree. (probably due to cis-trans
isomerism). Alternatively 10 g. III refluxed 3 hrs. in 180 ml. C6H6 with
3.8 ml. piperidine and 30 mg. p-MeC6H4SO3H gave 9.3 g. V. III (1 g.)
refluxed with 0.5 g. fused NaOAc and 50 ml. Ac2O gave 22-
acetoxymethylretrobisnorchola-4,20(22)dien-3-one (VI). V (300 mg.) in 4.5 ml.
C6H6 added in 45 min. at +5.degree. to +5.degree. to 453 mg. Na2C2O7.2H2O
in 4.5 ml. AcOH and 3 ml. C6H6 and the product worked up gave 150 mg.
retroprogesterone (VII), m. 163-4.degree. (CH2Cl2-ligno), [.alpha.]2D

-62.degree.. III treated with NaOAc in Ac₂O gave VI and VI ozonized, decompd., and hydrolyzed gave VII. VII (10 g.) in 79 ml. C₆H₆ stirred 1.5 hrs. with NaOMe in diethyl oxalate and some C₆H₆ gave 10.8 g. Na enolate of 21-ethoxyxalyretroprogesterone (VIII). VIII in 150 ml. MeOH treated 40 min. at -20 with 5.9 g. iodine in 210 ml. MeOH, mixt. stirred 1.5 hrs., and the iodine compd. decompd. with NaOMe soln. gave 5.55 g. 21-iodoretroprogesterone (IX). (5.55 g.) refluxed 18 hrs. in 200 ml. Me₂CO with 12 g. KOAc and chromatographed on Al₂O₃ gave 335 mg. retrodeoxycorticosterone acetate, m. 165.8.degree. (alc.). V (9.6 g.) in 475 ml. CH₂Cl₂ treated dropwise at -55.degree. with 4.08 g. Br in 50 ml. CH₂Cl₂, the dibromo compd. stirred 2 hrs. at 20.degree., the 2-bromo deriv. heated 1 hr. at 70.degree. with 70 ml. C₅H₅N, then 0.5 hr. at 100.degree., and worked up gave 6 g. 3-oxoretrobisnorchol-4,17(20)-dien-22-al (X), m. 155.9.degree. (Me₂CO-alc.). [alpha;]_D²³D -138.degree.. III (7.7 g.) in 100 ml. CCl₄ treated with 48 ml. Br soln. in CCl₄ (0.515 mole/ml.) and 3 g. CaCO₃ and then treated with C₅H₅N gave 7.15 g. X (5 g.) suspended with 8 g. NaCN in 50 ml. MeOH at -20.degree., left 2 hrs. at 20.degree. with 7.1 ml. AcOH, then 40 hrs. at 5.degree., and worked up gave the 22-HCN addn. product of X which treated at -80.degree. with O₃ gave 1.48 g. retroandrostan-4-en-3,17-dione (XI), m. 154.6.degree. (alc.). XI (3.03 g.) in 25 ml. C₆H₆ and 25 ml. Et₂O left 16 hrs. with 1.61 g. K in liquid NH₃ which had been treated with CH₃pbond.CH gave 1.95 g. 17, alpha-ethynylretrotestosterone (Xla), m. 195.6.degree. (hexane), [alpha;]_D²⁰D -219. 3-Oxoretrobisnorchola-4,6-dien-22-al (XII) (3.5 g.) in 50 ml. C₆H₆ refluxed 2.5 hrs. with 1.27 ml. piperidine and 20 mg. p-MeC₆H₄SO₃H gave 2.1 g. 22-(N-piperidyl)retrobisnorchola-4,6,20(22)-trien-3-one (XIII), m. 135.6.degree. (Me₂CO). XIII oxidized with Na₂Cr₂O₇ in AcOH gave 6-dehydroretroprogesterone (XIV), m. 168.9.degree. (Me₂CO). Lumisterone (3.95 g.) in 150 ml. CH₂Cl₂ and 0.81 ml. C₅H₅N treated with O₃ gave 3.11 g. 3-oxoretrobisnorchola-4,7-dien-22-al (XV), m. 196-200.degree. (CH₂Cl₂-Me₂CO). XV treated with piperidine and then oxidized with Na₂Cr₂O₇ gave 7-dehydroretroprogesterone (XVI). By isomerization of the 3-oxo-4,7-dehydro system of XVI with dry HCl XIV was obtained. VII (7.5 g.) in 500 ml. tert-BuOH refluxed 5 hrs. with 12.75 g. chloranil and the product chromatographed on Al₂O₃ gave XIV. I (3.95 g.) ozonized as described above gave 3.08 g. XII, m. 153.5.degree. (Me₂CO). 3-Oxoretrobisnorchola-4,20(22)-dien-22-al (0.978 g.) in 10 ml. C₆H₆ kept 4 hrs. at 0.degree. with 1.2 g. monoperphthalic acid in 25.5 ml. Et₂OAc gave 0.88 g. 17(20)epoxy-20-formyloxyretroprog-4-en-3-one (XVII). Hydrolysis of XVII with 2N NaOH gave 17, alpha-hydroxyretroprogesterone (XVIII), m. 222.5.degree. (alc.). XIII (6.5 g.) treated with Br and then with C₅H₅N gave 2.41 g. retrobisnorchola-4,6,17(20)-trien-3-one-22-al (XIX), m. 217-19.degree. (Me₂CO). XIX (15 g.) in 150 ml. Et₂OAc and 150 ml. C₆H₆ treated with 20.2 g. monoperphthalic acid in 450 ml. Et₂OAc and left 16 hrs. gave 16.4 g. resinous epoxy-20-formyloxy compd. which treated 1.5 hrs. at 30.degree. with 2N NaOH gave 5.69 g. 6-dehydro-17, alpha-hydroxyretroprogesterone (XX). XIX (3.7 g.) treated as above with 5.9 g. NaCN and MeOH followed by ozonization gave 1.2 g. retroandrosta-4,6-diene-3,17-dione, m. 189-90.degree. (Me₂CO). XVIII (220 mg.) and 220 mg. p-MeC₆H₄SO₃H in 15 ml. AcOH kept 18 hrs. at room temp. gave 130 mg. 3,17-diacetate of XVIII, m. 217-18.degree. (CH₂Cl₂-MeOH). XVIII (0.5 g.) similarly treated but in less Ac₂O and the product fractionally crystd. gave 260 mg. 17, alpha-acetoxyretroprogesterone, m. 171.3.degree. (MeOH). XVIII (900 mg.) treated with caproic anhydride and p-MeC₆H₄SO₃H, then with 0.3 ml. concd. HCl in 20 ml. alc., and the product chromatographed gave 67 mg. 17-caproate of XVIII, m. 50.3.degree. (hexane). Many esters of XVIII were similarly prepd. XVIII (0.495 g.) in tert-BuOH treated with chloranil gave 50 mg. XX, m. 242.5.degree. (alc.-hexane). 6-Dehydro-17, alpha-acetoxyretroprogesterone, m. 181.3.degree., was similarly prepd. Retropregesterone hydroxylated with Rhinospus nigricans gave a hydroxyretroprogesterone, m. 217-18.degree., and 17, alpha, 21-dihydroxyretroprogesterone (XXa) incubated with Aspergillus ochraceus gave retrohydrocortisone, m. 269.degree. (decompn.). Xla (1.88 g.) in 50 ml. C₅H₅N hydrogenated over 2 g. Pd-CaCO₃ gave 1.17 g. 17, alpha-vinyloxyretrotestosterone, m. 143.5-5.5.degree. (Me₂CO-hexane). VII (5 g.) in 250 ml. C₆H₆ refluxed 7 hrs. with 4 g. dichlorodicyanobenzoquinone and the product chromatographed on silica gel gave 2.14 g. 1-dehydroretroprogesterone, m. 154-5.5.degree. (Me₂CO-hexane). XIV (2.5 g.) gave 208 mg. dioxime, m. 279-82.degree. (tetrahydrofuran-ligroine). I (75 g.) and 55 ml. HCO₂Et in 1.2 l. C₆H₆ kept 3 days at room temp. with 16.5 g. NaH and the Na salt converted to the free alc. gave 2-hydroxymethylenelumista-4,6,22-trien-3-one (XX) as the hydrate, m. 119-22.degree., anhydrous form m. 122-3.5.degree.. Similarly, II gave 2-hydroxymethylenelumista-4,22-dien-3-one (XXI), m. 134-5.degree.. XXI (108 g. of Na salt) in 3.2 l. alc. treated 3.5 to 4.5 hrs. at 10.degree. with perchloryl fluoride gave 71 g. 2-fluorolumista-4,6,22-trien-3-one (XXII), m. 158-60.degree. (MeOH), [alpha;]_D²⁷D -635.degree. (alc.). XXII similarly gave 2-fluorolumista-4,22-dien-3-one. XXII (30.5 g.) in 610 ml. CH₂Cl₂ and 10 ml. C₅H₅N treated with O₃ at -80.degree. gave 16.6 g. 2-fluororetrobisnorchola-4,6-dien-3-on-22-al (XXIV), m. 183.5.degree. (CH₂Cl₂-Et₂O). XXIV (2.08 g.) similarly treated with piperidine and p-MeC₆H₄SO₃H gave 2-fluoro-22-(N-piperidyl)-retrobisnorchola-4,6,20(22)-trien-3-one, which with CrO₃ gave 2-fluoro-6-dehydroretroprogesterone, m. 153.4.degree. (alc.). Retropregnane-3,20-dione (XXV) (300 mg.) in alc. treated 3 hrs. at -20.degree. with 36.8 mg. CaCl₂·2H₂O and 16.3 mg. NaBH₄ gave retropregn-3-ol-20-one, m. 167-71.degree. (alc.-E+2O). VII (2.826 g.) in 150 ml. dioxane shaken with excess H over 0.3 g. 10% Pd-C in the presence of 0.6 g. KOH in 9 ml. MeOH gave XXV, m. 115-16.degree. (E+2O-hexane). XIV (5 g.), 7.5 g. chloranil, and 25 g. CaCO₃ refluxed 3 hrs. with 170 ml. isoamyl alc. and chromatography of the product gave XIV and 150 mg. 1,6-bisdehydroretroprogesterone (XXVI). XIV (5 g.) and 5.1 g. dihydroquinone in 250 ml. C₆H₆ refluxed 6 hrs. gave 1.52 g. XXVI, m.

143-3.5.degree. (Me₂CO-hexane). VII enol acetate (7.5 g.) and dioxane treated at room temp. with perchloryl fluoride gave 185 mg. 6, alpha-fluororetroprogesterone (XXVII), m. 150-1.degree. (Me₂CO-hexane), 1.16 g. 6, beta-fluororetroprogesterone (XXVIII), m. 163.5.degree. (MeOH), and 77 mg. 6-hydroxyretroprogesterone, m. 220-2.degree. (Me₂CO). XXVII (50 mg.) in 10 ml. CHCl₃ treated 1 hr. with passage of dry HCl gave XVIII. XVIII (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH treated at -4.degree. to 0.degree. with 1.5 g. iodine and the product refluxed with KOAc in Me₂CO gave 772 mg. 17, alpha, 21-dihydroxyretroprogesterone 21-acetate (XXIX), m. 218-238.degree. (decompn.) (Me₂CO). XX (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH similarly treated with iodine and the product refluxed with KOAc in Me₂CO gave 915 mg. 6-dehydro-17, alpha, 21-dihydroxyretroprogesterone 21-acetate, m. 238.5-44.degree. and 257.9.degree. (decompn.). XXIX (1.2 g.) in 30 ml. MeOH stirred 2 hrs. at 24.degree. with 216 mg. K₂CO₃ in 6 ml. H₂O gave 897.5 mg. XXa. Xla (3.12 g.) in 250 ml. dioxane reduced with H over Pd-CaCO₃ and the product chromatographed on silica gel gave 300 mg. 17, alpha-ethyl-5-retroandrostan-17-ol-3-one (A isomer), m. 125-6.5.degree. (Et₂O-petr. ether) and 828 mg. B isomer, m. 125-8.5.degree.. VII was converted to its 3-enol acetate, m. 90-2.degree. (MeOH). Retroandrosta-4,6-diene-3,17-dione (2.35 g.) in 70 ml. 2:1 mixt. C₆H₆-Et₂O stirred 0.5 hr. at -80.degree. with 1.28 g. K in 50 ml. liquid NH₃ previously treated with CH₃pbond.CH gave 6-dehydro-17, alpha-ethynylretrotestosterone, m. 205-7.degree. (Me₂CO-hexane). IX (6.6 g.) in 200 ml. MeCN and 5.72 g. AgF stirred 25 hrs. at 45.degree. gave 21-fluororetroprogesterone, m. 173-5.degree. (alc.-Me₂CO). XIV (10 g.) in 70 ml. C₆H₆ stirred 1.5 hrs. with 8.5 ml. (CO₂Et)₂ and 10.5 ml. of a 3.45N NaOMe soln. in MeOH, 70 ml. C₆H₆ and 3.2 ml. alc. gave 12.2 g. Na enolate of 21-ethoxyxaly-6-dehydroretroprogesterone (XXX). XXX in 170 ml. MeOH treated at -25.degree. with 7.2 g. iodine gave 12-iodo-6-dehydroretroprogesterone (XXXI). XXXI refluxed 5 hrs. with KOAc in Me₂CO, H₂O, and AcOH gave 6-dehydro-21-acetoxyretroprogesterone, m. 194.5-7.5.degree.. XIV (937 mg.) in 125 ml. CCl₄ treated in 50 min. with 0.5 g. Br in 10 ml. CCl₄ gave 4-bromo-6-dehydroretroprogesterone m. 121-2.degree. (MeOH) (decompn.). XIV with Cl similarly afforded 4-chloro-6-dehydroretroprogesterone, m. 185-6.degree.. 6-Chlororetroprogesterone (XXXII) (700 mg.) and 1 g. chloranil refluxed 30 hrs. in 100 ml. tert-BuOH gave 6-chloro-6-dehydroretroprogesterone, m. 165-6.degree. (alc.). 3-Acetoxyretropregna-3,5-dien-20-one (XXXIII) (1.85 g.) in 30 ml. Et₂O, 4 g. KOAc, 60 ml. 85% AcOH treated with 375 mg. Cl in 9.4 ml. AcOH gave XXXII, m. 197-9.5.degree. (Et₂O), and 3,6,20-trioxopregnane, m. 201-3.degree.. 6-Bromoretroprogesterone was similarly prepd., m. 138-40.degree. (decompn.). XIV (5 g.) reduced with NaBH₄ in alkali gave retropregna-4,6-diene-3,20-diol (XXXIV). XXXIV in C₆H₆ refluxed with 50 g. MnO₂ gave 3.27 g. retropregna-4,6-dien-20-ol-3-one, m. 198-8.5.degree. (Me₂CO), and a second C-20 isomer, m. 173-5.degree.. Retropregna-4-en-20-ol-3-one (XXXV) treated with NaH and HCO₂Et and the Na product acidified with 5% HCl gave 2-hydroxymethylenetetropregn-4-en-20-ol-3-one, m. 94-9.9.degree. (Et₂O), [alpha;]_D²¹D -155.degree. (alc.). VII (2 g.) in 40 ml. tetrahydrofuran reduced with LiAlH₄ gave retropregn-4-ene-3,20-diol and this product refluxed with MnO₂ in C₆H₆ gave 1.69 g. XXXV, m. 174-6.degree. (Me₂CO-hexane). XIV (1 g.) in 10 ml. CH₂Cl₂ treated with alc.-HCl gave 3-ethoxyretropregna-3,5,7-trien-20-one, m. 115-16.degree. (MeOH). XXXII (7.5 g.) in 200 ml. AcOH refluxed 4.5 hrs. with 21 g. KOAc gave 2-acetoxyretroprogesterone, m. 195-7.0.degree. (alc.). XXXIII treated with monoperphthalic acid in Et₂O gave 6-hydroxyretroprogesterone (XXXVI). Acetylation of XXXVI gave 6-acetoxyretroprogesterone, m. 177-8.5.degree. (alc.). XX was converted into the 17-caproate, m. 110-12.5.degree. (E₂O-hexane). 3,17-Diacetoxyretropregna-3,5-dien-20-one (13.2 g.) in 950 ml. dioxane and 40 ml. H₂O treated 1 hr. at room temp. with passage of perchloryl fluoride gave 6, alpha-fluoro-17, alpha-acetoxyretroprogesterone, m. 177-9.9.degree. (Me₂CO-hexane), and 6, beta-fluoro-17, alpha-acetoxyretroprogesterone, m. 197.5-8.5.degree. (Me₂CO), plus 3,6,20-trioxopregn-17, alpha-ol-17-acetate, m. 241-4.degree. (Et₂O-C₆H₆-Me₂CO). XIV (25 g.) treated with BzO₂H gave 6,7-oxidoretroprogesterone (XXXVII), m. 187-90.degree. (Et₂O), and some 6-chloro-7-hydroxyretroprogesterone (XXXVIII) due to splitting of the epoxide bond of XXXVII during chromatography. XXXVIII treated with HCl 3 hrs. at room temp. gave 6-chloro-6-dehydroretroprogesterone. XXVIII (4 g.) and 4 g. dichlorodicyanobenzoquinone in C₆H₆ refluxed 7.5 hrs. over 0.4 g. p-nitrophenol gave 2 g. 1,6-dihydro-6, beta-fluororetroprogesterone, m. 208-11.degree. (Et₂O). 17, alpha-Acetoxyretroprogesterone in MeOH treated 6 days with CuBr gave 6-dehydro-6-methoxy-17, alpha-acetoxyretroprogesterone, m. 275-80.degree. (alc.). XIV (3 g.) in 3 ml. thiopropionic acid refluxed 2.5 hrs. gave 7-acetylthioretroprogesterone, m. 133-5.degree. (Me₂CO-hexane). VII similarly treated with CuBr gave 6-dehydro-6-methoxyretroprogesterone, m. 208-8.degree.. XI (3 g.) in 30 ml. MeOH refluxed 10 min. with 1.6 ml. pyrrolidine gave 3.31 g. 3-(N-pyrrolidino)retroandrosta-3,5-dien-17-one (XXXIX). XXXIX (3.3 g.) refluxed 5 hrs. with a soln. contg. methylmagnesium chloride and worked up gave 2.52 g. 17, alpha-(2-methyl)retrotestosterone, m. 91-3.degree. (MeOH). Dried sample from Et₂O m. 106-8.degree.. I (60 g.) and 6 g. CuCl in 500 ml. tetrahydrofuran stirred 3 hrs. with soln. prep. from 100 ml. MeBr, 25 mg. Mg, and 5 g. CuCl in 200 ml. tetrahydrofuran gave 29 g. 7-methylumista-4,22-dien-3-one (XL), m. 94.5-5.5.degree. (ligroine). [alpha;]_D²²D -150.5.degree.. XL upon ozonation gave 3-oxo-7-methylretrobisnorchola-4-en-22-al (XL), m. 161.5-2.0.degree.. [alpha;]_D²³D -148. XL (4.65 g.) in 100 ml. C₆H₆ refluxed 5 hrs. with 2 ml. piperidine and 2 mg. p-MeC₆H₄SO₃H gave 7-methyl-22-(N-piperidyl)-retrobisnorchola-4,20(22)-dien-3-one (XLII), m. 153.5-4.5.degree.. [alpha;]_D²³D -120.degree.. XLII (1.96 g.) treated with Na₂Cr₂O₇ in AcOH gave 7-methylretroprogesterone, m. 208-8.degree.. [alpha;]_D²⁵D -57.degree.. XXXIX treated with CH₂CH₂MgCl gave 17, alpha-

allylretrotestosterone, m. 74-8.degree.. XX (1 g.) heated 45 min. at 80.degree. with 3.3 g. trimethylacetic acid and 1 ml. trifluoroacetic anhydride gave 6-dehydro-17.alpha.-hydroxyretroprogesterone 17-pimalate, m. 214-16.degree.. 17.alpha.-Acetoxyretroprogesterone (4 g.) refluxed 15 hrs. with 2.7 g. dichlorodicyanobenzoquinone in 200 ml. C6H6 gave 1-dehydro-17.alpha.-acetoxyretroprogesterone, m. 183-4.5.degree.. Xla treated with Ac2O-p-MeC6H4SO3H and then with concd. HCl in MeOH gave 17.alpha.-ethynylretrotestosterone 17-acetate, m. 183-4.degree. (Me2CO). VII by hydroxylation (microbiol.) gave 18.alpha.-hydroxyretroprogesterone (XLII), m. 172.5-4.5.degree., [alpha].25D -92.3.degree.. Dehydration of XLII gave 16-dehydro retroprogesterone, m. 165-7.degree.. Microbiol. hydroxylation of VII gave 15.alpha.-hydroxyretroprogesterone, m. 203-5.degree., [alpha].D -23.degree.. Oxidn. of 11,17.alpha.,21-trihydroxyretroprogesterone 21-acetate with CrO3 gave retrocortisone 21-acetate, m. 275.degree. (decompn.). Microbiol. hydroxylation of XIV gave 6-dehydro-16.alpha.-hydroxyretroprogesterone (XLIV), m. 200-3.degree., [alpha].D -526.degree.. Dehydration of XLIV gave 6,18-bisdehydroretroprogesterone, m. 163-5.degree.. Hydroxylation of VII gave 11-hydroxyretroprogesterone (XLV). Oxidn. of XLV with CrO3 gave 11-oxoretroprogesterone, m. 158-60.degree.. Hydroxylation of XVIII gave 11,17.alpha.-dihydroxyretroprogesterone (XLVI), m. 202-6.5.degree. (decompn.), [alpha].D -118.degree.. XLVI oxidized as above gave 11-oxo-17.alpha.-hydroxyretroprogesterone, m. 240-5.degree.. XXIII was converted into 2-fluoro-6-dehydro-17.alpha.-acetoxyretroprogesterone, m. 204-5.degree.. Degradation of the side-chain of 2-fluorodihydrocolumisterone gave 2-fluororetroprogesterone, m. 162-4.degree.. It was converted to 2-(ethoxyxalyl)lumista-4,22-dien-3-one then to 2-methylumista-4,22-dien-3-one (XLVII). XLVII ozonized, treated with Ac2O, and oxidized gave 2-methylretroprogesterone, m. 126-7.degree.. Degradation of the side chain of 2-methylumista-4,6,22-trien-3-one gave 2-methyl-6-dehydroretroprogesterone, m. 168.5-70.0.degree.. Retroandrost-4-en-17-one (XLVIII) treated with CH2:CHCl2MgCl gave 17.alpha.-allylretroandrost-4-en-17-ol, m. 79-86.degree.. XLVIII with KC.tpbond.CH in iso-PrOH gave 17.alpha.-ethynylretroandrost-4-en-17-ol, m. 74-5.degree.. Treatment of the Na enolate of the 21-ethoxy oxalate of XXVI with perchloryl fluoride in MeOH and NaOMe gave after refluxing with KOAc 21-fluoro-1,6-bisdehydroretroprogesterone, m. 154-5.degree.. XI (1.13 g.) reduced with 550 mg. LiAlH4 gave retroandrost-4-en-3,17.beta.-diol (XLIX), m. 117-18.degree. (lignore). Crude XLIX shaken 17 hrs. in 60 ml. CHCl3 with 6 g. MnO2 gave retrotestosterone (L), m. 115-6.degree. (Et2O), [alpha].D -23D -154.degree.. L gave the .beta.-phenylpropionate, m. 73-4.degree. (MeOH). L (5 g.) treated as above with chloranil 1.43 g. 6-dehydroretrotestosterone (L), m. 174-5.degree. (Et2O). L (360 mg.) afforded 233 mg. propionate, m. 115-17.degree. (MeOH). L (0.5 g.) treated with 0.5 g. Li in 75 ml. NH3 and 50 ml. Et2O and the product esterified gave 270 mg. bis(3,5-dinitrobenzoate) of retro-5-androstane-3,17.beta.-diol, m. 237-42.degree. (CH2Cl2-Me2CO). L (1 g.) in 35 ml. C6H6 refluxed 48 hrs. with 1 g. SeO2 and 0.6 ml. H2O and the product chromatographed on Al2O3 gave 98 mg. 1-dehydroretrotestosterone, m. 175-7.degree. (hexane-CH2Cl2). L (1.14 g.) was converted into enol of 2-(ethoxyxalyl)retrotestosterone (LII). LII (1.3 g.) refluxed 18 hrs. with 2 ml. MeI in 25 ml. Me2CO and 1 g. K2CO3 and chromatographed on Al2O3.

gave 207 mg. 2-methylretrotestosterone, m. 177-9.5.degree. (Et2O-hexane). Retroandrost-4,6-dien-3,17-dione (LIII) treated with LiAlH4 gave retroandrost-4,6-diene-3,17.beta.-diol (LII), m. 140-4 (decompn.). Crude LIII refluxed 30 hrs. with MnO2 in C6H6 gave 3 g. Li.

6-Bromoretrotestosterone 17-acetate treated with C5HSN gave 17-acetate of LI, m. 131-3.degree. L (1 g.) and 0.005 ml. concd. H2SO4 refluxed 3 hrs. with 5 ml. isopropenyl acetate gave 0.9 g. 3,17.beta.-diacetoxyretroandrosta-3,5-diene, m. 118-19 (MeOH). L (1 g.) added to 0.4 g. K in 20 ml. tert-BuOH, left 3.5 hrs. at room temp. with 1.3 ml. MeI gave 4,4-dimethylretroandrost-5-en-17.beta.-ol-3-one, m. 152.5-3.5.degree.. L gave the p-hexyloxyphenylpropionate and propionate (LIV), m. 107-8.degree.. LIV acetylated with isopropenyl acetate in the presence of traces of concd. H2SO4 gave 3-acetoxyretroandrosta-3,5-dien-17.beta.-ol 17-propionate, m. 102-4.degree.. 6-Bromoretrotestosterone 17-acetate (410 mg.) and 1.3 g. KOAc in 10 ml. AcOH refluxed 4 hrs. gave 2-hydroxyretrotestosterone 2,17-diacetate, m. 184-6.degree.. 3,17-Diacetoxyretroandrosta-3,5-diene treated with KOAc in AcOH, then with Br in AcOH, and worked up gave 6-bromoretrotestosterone 17-acetate, m. 130.degree. (decompn.). 3,17.degree..-Diacetoxyretroandrosta-3,5-diene (4 g.) in 178 ml. EtOAc contg. 14.3 mg. monoperphthalic acid/ml. left overnight at 5.degree.. gave mixt. (LV) of 6.alpha.- and 6-beta.-hydroxyretrotestosterone 17-acetate, m. 167-70.degree.. LV (2.6 g.) in 10 ml. C5HSN and 10 ml. Ac2O left 20 hrs. at room temp. and the product separated gave one isomer of 6,17-diacetoxyretrotestosterone, m. 178-80.degree., and the other isomer, m. 116-17.degree.. LI was converted to the 17-palmitate, m. 58.5-9.0.degree.. L treated with NaH and HCO2Et and then with 5% HCl gave 2-hydroxymethylenretrotestosterone (LVI), m. 98-120.degree. (aq. alc.). LVI (5 g.) in 13 ml. alc. refluxed 3 hrs. with 2.5 ml. N2H4.H2O in 40 ml. alc. gave 3.5 g. 17.beta.-hydroxyretroandrosta-4-eno[3,2-c]pyrazole, m. 259-63.degree., [alpha].D -24D -149.degree. (alc.). LI (2 g.) in 10 ml. pyridine left 18 hrs. at room temp. with 2.5 g. p-hexyloxyphenylpropionyl chloride gave 3.9 g. resinous 6-dehydroretrotestosterone 17-(p-hexyloxyphenylpropionate). LI treated 16 hrs. at 60.degree. with succinic anhydride gave the 17-hemisuccinate, m. ***17*** -93.5-201. ***5*** -203.5.degree.. LI also gave the 17-phenylpropionate, m. 93-4.degree. (MeOH). LII treated with Br in CCl4 gave 4-bromoretroandrosta-4,6-dien-3,17-dione, m. 130-50.degree.. L 17-propionate (1.2 g.) in 150 ml. C6H6 treated with 9 ml. (CH2O)2 gave 3,3-ethylenedioxyretroandrosta-3,5-dien-17.beta.-ol-17-propionate, m.

66-8.beta.. XXXIX (3 g.) treated with MeMgBr gave 17.alpha.-methylretrotestosterone (LVII), m. 133-4.degree.. LII similarly gave 3-ethoxyretroandrosta-3,5,7-trien-17-one, m. 118-19.5.degree.. LII (1 g.) in 15 ml. CH2Cl2 left 0.5 hr. at 0.degree. with dry HCl in MeOH gave 404 mg. 3-methoxyretroandrosta-3,5,7-trien-17-one, m. 139-40.degree.. L (2.5 g.) converted to the 17-hexahydrobenzoate, m. 71-3.degree. (petr. ether). LVII (2 g.) and dichlorodicyanobenzoquinone in C6H6 refluxed 7 hrs. gave 1-dehydro-17.alpha.-methylretrotestosterone, m. 163-4.degree.. XI treated with isopropenyl acetate gave 3-acetoxyretroandrosta-3,5-dien-17-one, m. 142-3.degree.. L (1.564 g.) in 6.25 ml. C5HSN treated 24 hrs. at room temp. with 1.56 g. p-toluenesulfonyl chloride gave the 17-tosylate, m. 164.5-5.5.degree.. The tosylate treated with KOAc in HCONMe2 and the resin washed with KOH soln. gave retroandrosta-4,16-dien-3-one and L was converted into the 17-acetate, m. 128.5-30.0.degree.. 3,17.beta.-Diacetoxyretroandrosta-3,5-diene (10.3 g.) treated in dioxane with perchloryl fluoride and chromatographed on silica gel gave 6,18-alpha.-fluororetrotestosterone 17-acetate, m. 129.5-30.5.degree.. Microbiol. hydroxylation of L gave 16.alpha.-hydroxyretrotestosterone, m. 210-12.degree., [alpha].D -187.degree.. XXIII converted into 2-fluororetrobisnorcholesterol, m. 128-6.degree.. 2-fluororetrotestosterone, and finally 2-fluoro-6-dehydroretrotestosterone, m. 90-5.degree. and 142-3.5.degree.. XI reduced with NaBH4 in Et2O gave 3,17.beta.-dihydroxyretroandrosta-17-one (LVIII), m. 156-8.degree.. LVIII oxidized with CrO3 in Me2CO contg. H2SO4 gave retro-5-androstane-3,17-dione, m. 114-15.5.degree.. 17.alpha.-Methylretroandrosta-4-en-17-ol was obtained by treatment of retroandrosta-4-en-17-one (LIX) with MeMgI. L (2 g.) in 3 ml. Et2O and 6.5 ml. AcOH stirred 1 hr. with 0.72, ml. 1,2-ethanedithiol and 0.85 ml. BF3.Et2O gave 3-ethylene dithioketal of L, m. 166-7.5.degree.. This ketal (0.5 g.) in 2.5 ml. tetrahydrofuran added to 15 ml. liquid NaOH and 5 ml. tetrahydrofuran, stirred 15 min. with 0.4 g. L gave 3-deoxyretrotestosterone (LX). LX oxidized with CrO3 in Me2CO gave LIX, m. 89-90.5.degree.. L with AcCl gave the 17-acetate, m. 113-14.50. LXII (1 g.) in 50 ml. CH2Cl2 treated in 20 min. at -55.degree. with 0.15 ml. Br in 6 ml. CH2Cl2, mixt. heated to 0.degree., and product heated with C5HSN for 1 hr. at 70.degree. gave 7-methylretrobisnorchola-4,17(20)-dien-3-on-22-ol (LXI), m. 182-3.5.degree.. LXI suspended in MeOH treated with NaCN, AcOH, and MeOH 2 hrs. from -20.degree. to +5.degree. and kept 40 hrs. at 5.degree. gave 7-methylretroandrosta-4-ene-3,17-dione (LXII), m. 196-7.degree.. LXII was reduced to give 7-methylretroandrosta-4-ene-3,17.beta.-diol (LXIII), m. 80-95.degree.. LXIII oxidized as above gave 7-methylretrotestosterone, m. 146.5-50.0.degree.. 3,17.beta.-Diacetoxyretroandrosta-3,5-diene (3 g.) in 60 ml. Et2O treated with 6.4 g. KOAc in 120 ml. 85% AcOH, and treated 5-10 min. at 0.degree. with 0.57 g. Cl gave 6-chlororetrotestosterone 17-acetate, m. 176-8.degree.. It treated with Et orthoformate in C6H6 and alc. gave 3-ethoxylumista-3,5,22-triene (LXIV), m. 76-7.5.degree. (alc.). LXIV (12.7 g.) in 60 ml. dioxane and 4.8 ml. C5HSN left 45 hrs. at room temp. with 20 g. CBr4 gave 7.46 g. 6-tribromomethylhydrocolumisterone (LXV), m. 132-3.5.degree. (Me2CO-MeOH). LXV (100 mg.) in 15 ml. alc. heated with 15 ml. of a strong anion exchange resin gave 6-dibromomethylenedihydrocolumisterone, m. 100-2.5.degree., [alpha].D -23D 10.degree.. XI was converted into 3-(1-pyrrolidino)retroandrosta-3,5-dien-17-one (LXVI). LXVI treated with CH2:CH2MgCl gave 17.alpha.-[2-methyl-6-dehydroretrotestosterone, m. 106-8.degree.. Similarly LXVI gave 17.alpha.-allylretrotestosterone, m. 76-8.degree.. Retroandrosta-4,6-diene-3,17-dione was converted into 3,7-di(1-pyrrolidino)retroandrosta-3,5-dien-17-one, and then alkylated to give 6-dehydro-17.alpha.-[2-methyl-6-dehydroretrotestosterone. Many related compds. were prep'd. by the above described procedures.

L22 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2002 ACS
 AN 1964:3413 CAPLUS
 DN 60:3413
 OREF 60:602g-h,603a
 TI 6 ***Fluor*** - ***17*** .alpha.- ***alkyl*** -1,4-androstadien-17.beta.-ol-3-ones
 IN Campbell, J. Allan; Pederson, Raymond L.; Babcock, John C.; Hogg, John A.
 PA Upjohn Co.
 SO 3 pp.
 DT Patent
 LA Unavailable
 PATENT NO. KIND DATE APPLICATION NO. DATE

 PI DE 1139838 19621122 DE
 PRAI US 19571129
 GI For diagram(s), see printed CA Issue.
 AB The title compds., superior gonadotropic agents, were prep'd. from the corresponding 4-enes by dehydrogenation (fermentation, e.g. with Septomyxa affinis, or chem., e.g. with SeO2), followed by acylation and (or) epimerization to the 6,18-alpha.-fluoro compd., as exemplified by 6,18-alpha.-fluoro-17.alpha.-methyl-1,4-androstadien-17.beta.-ol-3-one (I), m. 161-63.degree. (CH2Cl2-hexane).

L22 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1962:469449 CAPLUS

DN 57:69449

OREF 57:13843e-i,13844a-c

TI 17.alpha.,21-Epoxypregnenes

IN Spero, George B.; Lincoln, Frank H., Jr.; Schneider, William P.

PA Upjohn Co.

SO 3 pp.
 DT Patent
 LA Unavailable
 PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 3012028 19611205 US 19590526
 AB A cold soln. of 85 mg. MeSO₂Cl in 1 ml. of pyridine was added to 200 mg. of 6.alpha.-methyl-9.alpha.-fluorocortisone in 1 ml. pyridine at 0.degree.. This mixt. was kept 3 hours between 0.degree. and 5.degree.. Ice and sufficient dil. HCl to neutralize the pyridine was added and the mixt. extd. with CH₂Cl₂. The exts. were washed with cold NaHCO₃ soln, dried, and evapd. under reduced pressure to give 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.,21-dihydroxy-4-pregnene-3,11,20-trione 21-methanesulfonate (I). Similarly 1-dehydro-6.alpha.-methyl-9.alpha.-fluorocortisone gave 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.,21-dihydroxy-1,4-pregnadiene-3,11,20-trione 21-methanesulfonate (II). II in 18 ml. Me₂CO was treated with a soln. of 250 mg. of NaI in 6 ml. Me₂CO. This mixt. was refluxed with stirring for 15 min., cooled, and evapd. to dryness under reduced pressure to give 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.-hydroxy-21-iodo-4-pregnene-3,11,20-trione. Similarly, II, gave 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.-hydroxy-21-iodo-1,4-pregnadiene-3,11,20-trione (III). A suspension of 3.8 g. KF in a soln. of 7.7 g. 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.,21-trihydroxy-4-pregnene-3,20-dione 21-methanesulfonate (IV) in 80 ml. Me₂SO was stirred and heated on a steam bath 16 hrs. The mixt. was cooled, dill. with 500 ml. of HO, and extd. with CH₂Cl₂. The exts. gave a solid which was chromatographed on 200 g. of Florisil. The column was eluted with CH₂Cl₂ and mixts. of acetone (10 to 15%) in Skellysolve B. The material eluted with the acetone and Skellysolve B was extd. with acetone-Skellysolve B. The ext. was evapd. and the residue combined with the material eluted with CH₂Cl₂. This was chromatographed on Florisil and the column eluted with acetone (5 to 15%) in Skellysolve B. The material eluted with 10% acetone in Skellysolve B was recrystd. to give 4.8 g. 6.alpha.-methyl-9.alpha.-fluoro-11.beta.-hydroxy-17.alpha.,21-epoxy-4-pregnene-3,20-dione (V), m. 208.5.degree., v 3340, 1802, 16371600, 960, 870 cm.⁻¹ Similarly a soln. of 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.,21-dihydroxy-4-pregnene-3,11,20-trione 21-toluenesulfonate in HCONMe₂ heated with KF gave 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.,21-epoxy-4-pregnene-3,11,30-trione (VI). Similarly, 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.,21-trihydroxy-1,4-pregnadiene-3,20-dione 21-methanesulfonate gave 6.alpha.-methyl-9.alpha.-fluoro-11.beta.-hydroxy-17.alpha.,21-epoxy-1,4-pregnadiene-3,20-dione (VII), m. 238-43.degree. [α_D] 150.degree. (acetone). Similarly, II gives 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.,21-epoxy-1,4-pregnadiene-3,11,20-trione (VIII). Other 6.alpha.- and 6.beta.- "alkyl" -9.alpha.- "fluoro" -11.beta., "17" -11.beta., "17" -11.beta., 21-trihydroxy-1,4-pregnadiene-3,20-dione 21-sulfonates and their 11-oxo analogs react similarly to the corresponding 17.alpha.,21-epoxides. A mixt. of freshly prep. Ag₂CO₃, 14 g. of 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-21-iodo-4-pregnene-3,20-dione and 270 ml. MeCN were stirred and refluxed for 2 hours. The mixt. was cooled and filtered through Celite. The Celite was washed with hot MeCN; these washings were added to the filtrate. The dried filtrate was evapd. to dryness to give 12.3 g. of residue which was chromatographed on 900 g. of acid-washed alumina. The column was eluted with EtOAc (1 to 10%) in benzene. The material eluted with 10% acetone was recrystd. from acetone to give V. Similarly, 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-21-iodo-1,4-pregnadiene-3,20-dione yielded VII and III yielded VIII. V, VI, VII, VIII, and similar compds. have diuretic and antinflammatory activity.

L22 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2002 ACS
 AN 1962:448821 CAPLUS
 DN 57:48821
 OREF 57:9659h-i,9660a-c
 TI Organic fluorine compounds. XXVI. The synthesis of fluorine compounds from sulfonic acid esters
 AU Bergmann, Ernst D.; Shahak, I.
 CS Hebrew Univ., Jerusalem
 SO Bull. Res. Council Israel Sect. A (1961), 10, 91-9
 DT Journal
 LA Unavailable
 AB cf. CA 56, 12728f. Alkyl sulfonates were prep'd. from the corresponding alkoxides and PhSO₂Cl or p-MeC₆H₄SO₂Cl. A mixt. of 150 ml. diethylene glycol and 45 g. KF was dehydrated by heating at 100-10.degree. 30 min. with stirring. 0.5 mole of the alkyl sulfonate was added and the mixt. heated cautiously to 130-50.degree., depending on the b.p. of the fluoride formed, which was distd. over if boiling below 150.degree. or extd. with CHCl₃. n-Pentyl, n-hexyl, n-heptyl, n-octyl, lauryl, and cetyl fluoride, 4-fluoromethyl-2,2-dimethyl-1,3-dioxolane (b. 133-4.degree.), 2-ethyl-4-fluoromethyl-2-methyl-1,3-dioxolane, Et. alpha.-fluoropropionate, and Et fluorooacetate were obtained in good yields (55-95%). Poorer yields (5-35%) were given by: 2-octyl fluoride, 1,3-dichloro-2-fluoropropane (b. 126.degree.); bis(beta-fluoroethyl)ether; 5-fluoro-1,3-dioxane (b. 103-5.degree.); 4-fluoromethyl-1,3-dioxolane (b. 111-12.degree.); 5-fluoro-2-phenyl-1,3-dioxane (b30 117-19.degree.); 4-fluoromethyl-2-phenyl-1,3-dioxolane (b30 111-14.degree.). In a second procedure, triptylamine was neutralized with 40% HF and dried, giving probably C₈H₁₇NH₂HF, and fluorides were obtained from "alkylsulfonates" in "17" -52% yields. .alpha.- "Fluoronitriles" were obtained from aldehydes as follows: 0.6 mole of aldehyde, 25 g. NaCN (or 35 g. KCN) in aq. soln. treated with 0.5 mole PhSO₂Cl in 120 ml. CH₂Cl₂ at 15.degree. with stirring for 1 hr. and at 25.degree. 6 hrs. Org. layer sep'd., washed (H₂O and aq. NaHSO₃),

dried, concd., and treated with KF gave fluoroacetonitrile (30%), .alpha.-fluoropropionitrile (b. 95.6.degree., 52%); .alpha.-fluorobutyronitrile (b. 115-16.degree., 58%); .alpha.-fluorovaleronitrile (b. 137-8.degree., 49%); .alpha.-fluoroisovaleronitrile (b. 126-7.degree., 60%); .alpha.-fluorocapronitrile (b. 132-3.degree., 57%). Alkyl-p-toluenesulfonates gave corresponding Cl, Br, I, CN, or CNS derivs. in similar procedures using LiCl, NaBr, NaI, KCN, or KCNS, in 72-96% yields.

L22 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1959:51316 CAPLUS
 DN 53:51316
 OREF 53:9297b-i,9298a-d

TI 6-Methyl-9.alpha.-fluoro-11-oxygenated pregnenes
 IN Lincoln, Frank H., Jr.; Schneider, Wm. P.; Spero, Geo. B.
 PA Upjohn Co.

DT Patent
 LA Unavailable
 FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2867638 19590106 US
 DE 1058990 DE
 GB 653777 GB
 AB The prepn. of 6-hydrocarbyl substituted steroids was described. 6.alpha.-Methyl-9.alpha.-fluorohydrocortisone (1 g.) (cf. Spero, et al., C.A. 51, 11369h) and 10 ml. pyridine (I) cooled to 0.degree., 0.5 ml. Me₂SO₂Cl added, the soln. kept at 0-5.degree. 18 hrs., ice and 10 ml. H₂O added, and then 120 ml. 5% HCl ptd. 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.,21-trihydroxy-4-pregnene-3,20-dione 21-methanesulfonate (II), m. 166-78.degree. (decompr.). II (750 mg.) dissolved in 15 ml. acetone (III), refluxed with stirring 15 min. with 750 mg. NaI in 15 ml. III, and the soln. concd. to dryness in vacuo gave 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.,21-iodo-4-pregnene-3,20-dione (IV). IV stirred with 15 ml. HOAc 45 min., 750 mg. Zn dust added and stirring continued 20 min., the mixt. filtered, the filtrate dill. with methylene chloride and washed with aq. K₂CO₃ until neutral, the org. layer sep'd., dried, concd. to 25 ml., and chromatographed over 40 g. Florisil gave 16 100 ml. fractions (1 through 15 with Skellysolve B-hexane-10% III, and 16 with III). Fractions 5 through 16 combined and evapd. gave 80.3% 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-4-pregnene-3,20-dione (V), m. 237-29.degree. (from III-Skellysolve B-hexanes), [α_D]D 103 degree. (in III). V (1.3 g.), 100 mg. chromic anhydride, 10 ml. glacial HOAc, and 0.5 ml. H₂O kept 8 hrs. at room temp., poured into 50 ml. ice H₂O, and neutralized with dil. NaOH ptd. 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.-hydroxy-4-pregnene-3,11,20-trione (VI) (crystd. from EtOAc and Skellysolve B-hexanes). In a similar manner to the prepn. of II, other 6.alpha.-alkyl(or .alpha.-aryl)-9.alpha.-fluorohydrocortisones or the corresponding fluorocortisones treated with the chlorides or bromides of toluenesulfonic acid, methanesulfonic acid, or other org. sulfonic acids gave the corresponding 21-substituted derivs. These compds. treated as in the prepn. of IV yielded the corresponding 21-iodo compds., such as 6.alpha.-ethyl-9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-21-iodo-4-pregnene-3,20-dione (or the corresponding Pr, iso-Pr, Bu, iso-Bu, pentyl, Pr compds.), or 6.alpha.-methyl-9.alpha.-fluoro-17.alpha.-hydroxy-21-iodo-4-pregnene-3,11,20-trione (or the corresponding Et, Pr, iso-Pr, Bu, iso-Bu, pentyl, hexyl compds.). Treating the diones or triones thus obtained by the process used in the prepn. of V (or with Na bisulfite or thiosulfate) yields the corresponding 6.alpha.- "alkyl" -9.alpha.- "fluoro" -11.beta., "17" -11.beta., "17" -11.beta., .alpha.-dihydroxy-4-pregnene-3,20-diones or 6.alpha.- "alkyl" -9.alpha.- "fluoro" -11.beta., "17" -11.beta., "17" -11.beta., .alpha.-hydroxy-4-pregnene-3,11,20-triones. Instead of the 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.-fluorohydrocortisone (or cortisone) the 6.beta.-epimer can be used in this series of reactions. If the reaction conditions are kept near neutrality, the corresponding 6.beta.-epimers are formed, which yield the 6.alpha.-epimers on treatment with acid or base in an org. solvent. 6.alpha.-Methyl-11.beta.,17.alpha.-dihydroxy-4-pregnene-3,20-dione (1 g.), 650 mg. N-bromoacetamide, and 6 ml. I₂ stirred in the dark 30 min., cooled in ice, a stream of SO₂ directed onto the surface of the stirred mixt. until a neg. KI-starch test was obtained, 50 ml. H₂O added, and the mixt. maintained at 5.degree. 30 min. ptd. 0.75 g. 6.alpha.-methyl-17.alpha.-hydroxy-4,9(11)-pregnadiene-3,20-dione (VII). VII (0.5 g.) dissolved in 20 ml. methylene chloride, 1 ml. 71% perchloric acid in 10 ml. H₂O and 200 mg. N-bromoacetamide in 50 ml. t-BuOH added, the mixt. maintained at room temp. 15 min., mixed with 0.3 g. Na sulfite in 12 ml. H₂O, the resulting mixt. distd. in vacuo until the residual soln. became cloudy, and 100 ml. ice H₂O added ptd. 6.alpha.-methyl-9.alpha.-bromo-11.beta.,17.alpha.-dihydroxy-4-pregnene-3,20-dione (VIII) (crystd. from III-Skellysolve B-hexane). VIII (0.45 g.), 0.45 g. anhyd. KOAc, and 20 ml. III refluxed 5 hrs., cooled, poured into H₂O, extd. with methylene chloride, the ext. dried, chromatographed on 25 g. Florisil, and the column developed with Skellysolve B-hexane contg. increasing amts. of III yielded 6.alpha.-methyl-9(11)-oxido-17.alpha.-hydroxy-4-pregnene-3,20-dione (IX) in the eluate contg. 10% III. IX (1 g.) in 50 ml. methylene chloride, 5 ml. 48% HF, and 0.5 ml. 71% perchloric acid stirred 6 hrs. and poured into excess cold aq. 5% NaHCO₃, the org. layer dried, and chromatographed as in the prepn. of IX gave V. Other 6.alpha.-alkyl(or aryl)-11.beta.,17.alpha.-dihydroxy-4-pregnene-3,20-diones or the 6.beta.-epimers will react similarly to give the corresponding 9.alpha.-fluoro derivs. (X). X oxidized with chromic anhydride as in the prepn. of VI yielded 6.alpha.-alkyl(or aryl)-9.alpha.-fluoro-17.alpha.-hydroxy-4-pregnene-3,11,20-triones; the 6.beta.-epimers react similarly. V (2 g.), 1 g. 3-oxobisnor-4-cholen-22-

al, and 115 ml. dimethylformamide added to a growing culture of *Septomyxa affinis* (ATCC 6737) and incubated 24 hrs., the steroid material extd. from the filtrate with methylene chloride, the ext. evapd. to dryness, chromatographed on a Florisil column, and the column developed with 5 fractions each of methylene chloride, Skellysolve B-III mixtures (9: 1, 8:2, 7:3, 1:1), and MeOH gave 6.alpha.-methyl-9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-1,4-pregnadiene-3,20-dione (recrystd. from III, m. 292-303 degree.) from the 7:3 Skellysolve B-III fraction. V and VI (and their 6.beta.-epimers) cause a loss of salt and water and also possess antiinflammatory, glucocorticoid, uterine, ovarian, and adrenal growth-depressional and adrenocorticoid activity. They are used in oral, parenteral, and topical compns.; in the latter case, incorporation of an antibiotic in the ointment has therapeutic advantages.

L22 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS

AN 1959:17487 CAPLUS

DN 53:17487

OREF 53:3298c-i

TI 6-Fluoro-17.alpha.-alkynyl-4-androstenes

IN Herr, Milton E.; Babcock, John C.; Campbell, J. Allan; Hogg, John A.; Pederson, Raymond L.

PA Upjohn Co.

DT Patent

LA Unavailable

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2838549 19580610 US
GB 893149 GB

AB The prepn. of 6-fluoro-11.beta.,17.beta.-dihydroxy-17.alpha.-ethynyl-4-androsten-3-one (I), 6-fluoro-11.beta.,17.beta.-dihydroxy-17.alpha.-ethynyl-19-nor-4-androsten-3-one (II), 6-fluoro-17.beta.-hydroxy-17.alpha.-ethynyl-4-androsten-3,11-dione (III), 6-fluoro-17.beta.-hydroxy-17.alpha.-ethynyl-19-nor-4-androsten-3,11-dione (IV), the 17-acylates, and intermediates is described. 6-Fluoro-11.beta.-hydroxy-3-(N-pyrrolidinyl)-3,5-androstan-17-one (2.25 g.) in 80 ml. anhyd. tetrahydrofuran added to a liquid NH3 soln. contg. CH₃pbond.CK, the mixt. kept in the cold several hrs., dild. with NH4Cl soln., extd. with Et2O, concd., the residue refluxed several hrs. in a buffered soln. of 6 g. NaOAc, 6 ml. H2O, 4 ml. AcOH, and 40 ml. MeOH, the mixt. extd. with Et2O, washed, evapd., and the residue in CH₂Cl₂ chromatographed on Florisil gave the 6.alpha.-isomer of I. The 6.beta.-form was present in the mother liquors and could be sepd. by addnl. chromatography followed by crystn. Similarly, substituting K alkylacetyldes was productive of the corresponding 6- ***fluoro***-11.beta.-hydroxy- ***17***.alpha.- (***alkylethynyl)***-testosterone. The 6.alpha.-form of I (1 g.) refluxed with (EtCO)2O yielded 6.alpha.-fluoro-11.beta.,17.beta.-dihydroxy-17.alpha.-ethynyl-4-androsten-3-one 17-propionate (V). Similarly the 6.beta.-form of I gave the 6.beta.-isomer of V. Similarly, 6-fluoro-11.beta.-hydroxy-3-(N-pyrrolidinyl)-19-nor-3,5-androstan-3-one with KC₃pbond.CH in NH₃, treated with aq. NH4Cl, and the resulting enamine hydrolyzed with NaOAc, AcOH, H₂O, and MeOH gave II. The substitution of K alkylacetyldes gives the corresponding 17.alpha.-alkylethynyl derivs. In the same manner as described above II may be converted to its 17-propionate or other 17-acylates. I (0.425 g.) in 20 ml. AcOH left several hrs. at 25 degree. with 0.25 g. CrO₃, 1 ml. H₂O, and 20 ml. AcOH gave 6.alpha.-form of III. In like manner the 6 beta.-form of III was prepnd. Similarly other 17.alpha.-alkylethynyl derivs. of I are oxidized to give the corresponding analogs of III. III (6.alpha.-form, 1 g.) with (EtCO)2O gave the 17.alpha.-propionate (VI). The 6.beta.-form of VI is similarly prepnd. from the 6.beta.-form of III. In the same manner shown above other 17-acylates of III are prepnd. Also the 17-propionates of the 17.alpha.-alkylethynyl analogs of III are similarly prepnd. II (6.alpha.-form) oxidized as above with CrO₃ gave IV (6.alpha.-form). The 6.beta.-form of IV was similarly obtained by oxidation of the 6.beta.-form of II. Similarly the 17.alpha.-methylthynyl and other 17.alpha.-alkylethynyl analogs of II were oxidized to give the corresponding 17.alpha.-alkylethynyl analog of IV. IV (6.alpha.- or 6.beta.-form) may be converted to the 17-propionate or to other 17-acylates. The 17-propionates of 6- ***fluoro*** -17.beta.-hydroxy- ***17***.alpha.- ***alkylethynyl*** -19-nor-4-androstan-3,11-diones may be similarly obtained.

=> d his

(FILE 'HOME' ENTERED AT 11:18:52 ON 06 JUN 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:19:22 ON 06 JUN 2002

L1 2613 S FERTILITY (3A) TREAT?

L2 78848 S CONTRACEPT?

L3 81300 S L1 OR L2

L4 142 S ENDOMETRIUM (3A) MATUR?

L5 81423 S L3 OR L4

L6 19 S L4 AND L3

L7 29173 S PROGEST? (3A) RECEPTOR?

L8 1077 S (ANTAGONIST OR INHIBIT?) (3A) L7

L9 0 S 17 ALPHA FLUORALKYL?

L10 0 S 17 FLUORALKY?

L11 8 S 17 (3A) FLURO?

L12 3684 S 17 (3A) FLUOR?

L13 15 S L12 (3A) ALKYL?

L14 0 S L13 AND L8

L15 69 S L8 AND L3
L16 1 S L15 AND L6
L17 33312 S CONCEPTION?
L18 35752 S L17 OR L1
L19 0 S L18 AND L4 AND L8
L20 1 S L8 AND L4
L21 8 DUP REM L6 (11 DUPLICATES REMOVED)
L22 15 DUP REM L13 (0 DUPLICATES REMOVED)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	ENTRY	SINCE FILE SESSION	TOTAL
FULL ESTIMATED COST		120.87	121.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	ENTRY	SINCE FILE SESSION
TOTAL		
CA SUBSCRIBER PRICE	-11.77	-11.77

STN INTERNATIONAL LOGOFF AT 11:44:55 ON 06 JUN 2002